VOLUME 80 • JULY 1959 • NUMBER 1

A.M.A. ARCHIVES OF

DERMATOLOGY

The Changing Pattern of Dermatology
G. A. Grant Peterkin

Calcinosis Cutis: Its Relationship to Scleroderma
Sigfrid A. Muller, Louis A. Brunsting, and R. K. Winkelmann

Generalized Rhinosporidiosis with Visceral Involvement
S. Agrawal, K. D. Sharma, and J. B. Shrivastava,

Psoriatic Arthritis
V. Wright

Defective Epidermal Utilization and Storage of S^{35} in Psoriasis
Morris J. Lipnik and Stanley H. Levy

Blood Histamine and Basophil-Eosinophil Counts in Skin Diseases
Herman J. Schultz, Charles F. Code, and Louis A. Brunsting

Investigations on the Effect of Psoralen Derivatives on Blood Sugar and Glutathione
Anwar El-Mofty, Abdel Monem El-Mofty, Hassan Abdelal, and M. F. S. El-Hawary

Hyperkeratosis Ichthyosiformis Congenita
Danilo Stevanovic and Sava Konstantinovic

Familial White Folded Dysplasia of the Mucous Membranes
Edward V. Zegarelli, Frank G. Everett, Austin H. Kutscher, John Gorman, and Norman Kupferberg

Histopathology of Pemphigus Foliaceus
Tancredo A. Furtado

Subcorneal Pustular Dermatosis
Robert E. Burns and Gerald Fine

Lichen Planus-like Eruption Caused by Color Developer
Orlando Canizares

A Case for Diagnosis, by Geoffrey Chaucer (13407-1400)
Marc Weiner

A Dermatologist's Trip to Japan
Stephen Rothman

The VII International Congress on Leprology
Paul Fasal

Meeting of the International Society for Human and Animal Mycology
Frederick Reiss

The Epidermal Biopsy
Robert P. Arthur and Walter B. Shelley

The Prismatic Binocular Microscope Adapted for Dermatologic Use
H. C. Goldberg and J. Kindler

A Bland Bath
Elmer R. Gross

The New, Newer, and Newest

Bronx Dermatological Society

Chicago Dermatological Society

Detroit Dermatological Society

Metropolitan Dermatological Society of Los Angeles

New York Dermatological Society

Philadelphia Dermatological Society

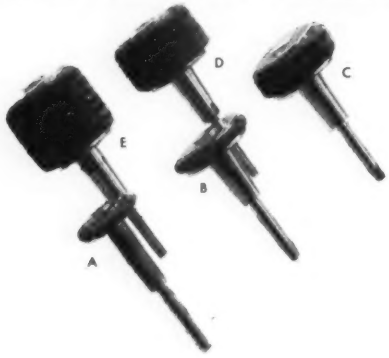
San Francisco Dermatological Society

Announcements

Books

AMERICAN MEDICAL ASSOCIATION PUBLICATION

ROBBINS INSTRUMENTS FOR COSMETIC DERMABRASION . . .

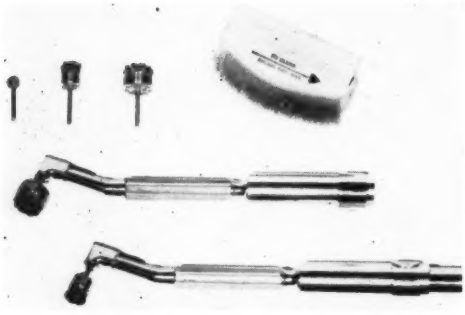


Give optimum results with a correct technique* in the obliteration of various skin disfigurements

KURTIN ORIGINAL PLANING BRUSHES
Patent No. 2,712,823**

A. EXTRA SMALL—2x12 mm.	$5.00
B. SMALL—2x18 mm.	5.00
C. MEDIUM—6x18 mm.	6.00
D. LARGE—10x18 mm.	7.00
E. EXTRA LARGE—14x18 mm.	8.00

In stainless steel with rounded cutting sides and REGULAR abrasive grades. B. SMALL BRUSH is also made in COARSE and FINE abrasive grades.

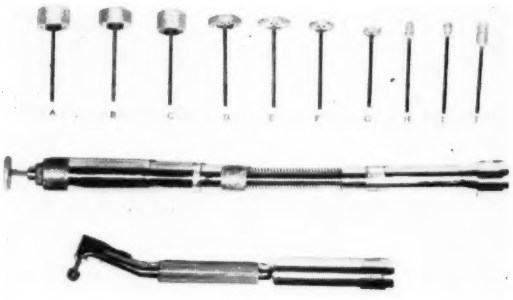


ROBBINS OWN CONTRANGLE BRUSHES (stainless) FOR PLANING WITH CONTRANGLE FLEXIBLE CABLE HANDPIECES. (Illustrated)

CONTRANGLE BRUSH—LARGE—15 mm.	$13.50
CONTRANGLE BRUSH—SMALL—10 mm.	10.50
CONTRANGLE DIAMOND FRAISE	6.50
CONTRANGLE HANDPIECE	20.50
CLEANING BRUSH (for stainless bristles comes with instructions)	1.50
CONTRANGLE ADAPTER for Pulley-Cord Engine Handpieces (not shown)	12.50

DIAMOND CHIP FRAISES FOR CUTANEOUS PROPHYLAXIS AND SUPERFICIAL ABRASION, AVAILABLE IN REGULAR and COARSE ABRASIVE GRADES

ILLUSTRATED	*REGULAR*	*COARSE*
A—17x10 mm.	$18.00	$35.00
B—17x8 mm.	18.00	30.00
C—15x10 mm.	15.00	25.00
D—17x4 mm.	10.00	20.00
E—17x2.5 mm.	8.50	16.50
F—13x2.5 mm.	8.50	15.00
G—10x2.5 mm.	8.00	15.00
H—Cone	6.50	12.50
I—Pear	6.50	12.50
J—Cylinder	6.50	18.00



*Write to Robbins concerning arrangements for demonstrations of dermabrasion without any obligation.

SERRATED STEEL WHEELS FOR SKIN GRATING and CUTTING

EXTRA LARGE—17x5 mm.	$3.00
LARGE—16x5 mm.	3.00
MEDIUM—11x4 mm.	3.00
SMALL—9x3 mm.	3.00

**Because the value of Robbins patented original planing brushes has been demonstrated many times in the past, one should beware of inferior imitations.

ROBBINS INSTRUMENTS COMPANY

Designers, Makers and Suppliers of Dermatological Specialties

CHATHAM, NEW JERSEY

TABLE OF CONTENTS

VOLUME 80 JULY 1959 NUMBER 1

ORIGINAL ARTICLES

PAGE

The Changing Pattern of Dermatology
G. A. Grant Peterkin, M.B.E., M.B., F.R.C.P.Ed., Edinburgh, Scotland 1

Calcinosis Cutis: Its Relationship to Scleroderma
Sigfrid A. Muller, M.D.; Louis A. Brunsting, M.D., and R. K. Winkelmann, M.D., Rochester, Minn. 15

Generalized Rhinosporidiosis with Visceral Involvement
S. Agrawal, M.B.B.S., M.Sc.Path., Jabalpur, India; K. D. Sharma, M.B.B.S., M.Sc.Path., Nagpur, India, and J. B. Shrivastava, M.D. (Bom.), D.B. (Lond.), Kasauli, India 22

Psoriatic Arthritis
V. Wright, M.D., M.R.C.P., Baltimore 27

Defective Epidermal Utilization and Storage of S^{35} in Psoriasis
Morris J. Lipnik, M.D., and Stanley H. Levy, M.D., Detroit 36

Blood Histamine and Basophil-Eosinophil Counts in Skin Diseases
Herman J. Schultz, M.D.; Charles F. Code, M.D., and Louis A. Brunsting, M.D., Rochester, Minn. 44

Investigations on the Effect of Psoralen Derivatives on Blood Sugar and Glutathione
Anwar El-Mofty, M.D.; Abdel Monem El-Mofty, M.D.; Hassan Abdelal, D.V.D., and M. F. S. El-Hawary, Ph.D. (London), Cairo, Egypt 53

Hyperkeratosis Ichthyosiformis Congenita
Danilo Stevanovic, M.D., M.Sc. (Cantab), and Sava Konstantinovic, M.D., Belgrade, Yugoslavia 56

Familial White Folded Dysplasia of the Mucous Membranes
Edward V. Zegarelli, D.D.S.; Frank G. Everett, D.M.D.; Austin H. Kutscher, D.D.S.; John Gorman, M.D., and Norman Kupferberg, B.S., New York 59

Histopathology of Pemphigus Foliaceus
Tancredo A. Furtado, M.D., Belo Horizonte, Brazil 66

Subcorneal Pustular Dermatosis
Robert E. Burns, M.D., and Gerald Fine, M.D., Detroit 72

Lichen Planus-like Eruption Caused by Color Developer
Orlando Canizares, M.D., New York 81

A Case for Diagnosis, by Geoffrey Chaucer (1340?-1400)
Marc Weiner, M.D., Washington, D. C. 87

Reports:

A Dermatologist's Trip to Japan
Stephen Rothman, M.D., Chicago 88

The VII International Congress on Leprology
Paul Fasal, M.D., San Rafael 91

Meeting of the International Society for Human and Animal Mycology
Frederick Reiss, M.D., New York 93

CLINICAL NOTES, NEW INSTRUMENTS AND TECHNIQUES

The Epidermal Biopsy
Robert P. Arthur, M.D., and Walter B. Shelley, M.D., Philadelphia 95

The Prismatic Binocular Microscope Adapted for Dermatologic Use
H. C. Goldberg, M.D., Plainfield, N. J., and J. Kindler, M.D., East Orange, N. J. 98

(Continued on next page)

A. M. A.
ARCHIVES OF DERMATOLOGY

VOLUME 80 JULY 1959 NUMBER 1

COPYRIGHT, 1959, BY THE AMERICAN MEDICAL ASSOCIATION

EDITORIAL BOARD

HERBERT RATTNER, Chief Editor

104 South Michigan Avenue, Chicago 3

HARVEY BLANK, Miami, Fla.
LOUIS BRUNSTING, Rochester, Minn.
J. LAMAR CALLAWAY, Durham, N. C.
A. C. CIPOLLARO, New York
GEORGE M. LEWIS, New York
H. E. MICHELSON, Minneapolis

J. F. HAMMOND, Editor, A. M. A. Scientific Publications

GILBERT S. COOPER, Managing Editor, Specialty Journals

TABLE OF CONTENTS (Continued)

A Bland Bath
Elmer R. Gross, M.D., Wilmington, Del. 99

THE NEW, NEWER, AND NEWEST 101

SOCIETY TRANSACTIONS

Bronx Dermatological Society 102
Chicago Dermatological Society 107
Detroit Dermatological Society 115
Metropolitan Dermatological Society of Los Angeles 119
New York Dermatological Society 121
Philadelphia Dermatological Society 122
San Francisco Dermatological Society 127

REGULAR DEPARTMENTS

Announcements 100
Books 130

Published monthly by the AMERICAN MEDICAL ASSOCIATION. Editorial and Circulation Offices: 535 North Dearborn Street, Chicago 10, Illinois. Publication Office: Thompson Lane, Box 539, Nashville 1, Tennessee.

Second-class postage paid in Nashville, Tennessee.

CHANGE OF ADDRESS: When there is a change of address, the Circulation Office of the American Medical Association should be notified at least six weeks before the change is made. The address label clipped from the subscriber's latest copy of the publication and a statement of old and new address should be included. If there is a postal zone number, it too should be included in the new address. The instructions should state whether the change is permanent or temporary.

TO PROTECT SKIN

AGAINST A WIDE RANGE OF IRRITANTS

- *in industry*
- *in the home*

Silicote provides an important advance in protecting skin from dry and aqueous irritants—prophylactically to prevent skin maceration, and therapeutically to exclude water, soap, and other substances from dermatoses that may be aggravated by them.

Clinical tests show that Silicote provides excellent protection against soap and water and soluble cutting oils.[1]

The protective property of Silicote is purely mechanical. Protective efficiency is necessarily determined by the nature and frequency of exposure. Frequency of application should be adjusted to provide adequate protection with minimum dosage.

SUGGESTED DOSAGE: Cleanse area thoroughly with soap and water. Apply thin film as required and rub in well. If skin is exposed constantly to irritant, apply every 2-4 hours, or as needed to provide protection. It is not necessary to remove original coat before applying subsequent coats. Any objectionable greasiness may be removed by wiping with a dry cloth, or washing gently with soap and water.

CONTRAINDICATIONS: Do not use on weeping or infected areas.

In Housewife's Eczema
Industrial Dermatoses
Chapping—Chafing
Intertrigo
Diaper Rash
Chronic Dermatoses
Aggravated by Soap
and Water

SILICOTE CONTAINS
30% dimethicone (silicone) in a specially prepared petrolatum base. Contains no water-soluble ingredients.

Send for samples and literature

1. Shaw, J. M., and Crowe, F. W.: Skin Protective Ointments. Arch. Dermat. & Syph. 71: 379, 1955.

SILICOTE
SILICONE OINTMENT

ARNAR-STONE LABORATORIES, INC. **MT. PROSPECT, ILLINOIS**

In Canada: Brent Laboratories, Ltd., Toronto

5/

Instructions to Contributors

Articles, book reviews, and other materials for publication should be addressed to the Chief Editor. Articles are accepted for publication on condition that they are contributed solely to this journal.

An original typescript of an article, with one carbon copy, should be provided; it must be double or triple spaced on one side of a standard size page, with at least a 1-inch margin at each edge. Another carbon copy should be retained by the author.

The main title of an article may not contain more than eighty characters and spaces; a subtitle may be of any length.

The author's name should be accompanied by the highest earned academic or medical degree which he holds. If academic connections are given for one author of an article, such connections must be given for all other authors of the article who have such connections.

If it is necessary to publish a recognizable photograph of a person, the author should notify the publisher that permission to publish has been obtained from the subject himself if an adult, or from the parents or guardian if a child. An illustration that has been published in another publication should be accompanied by a statement that permission for reproduction has been obtained from the author and the original publisher.

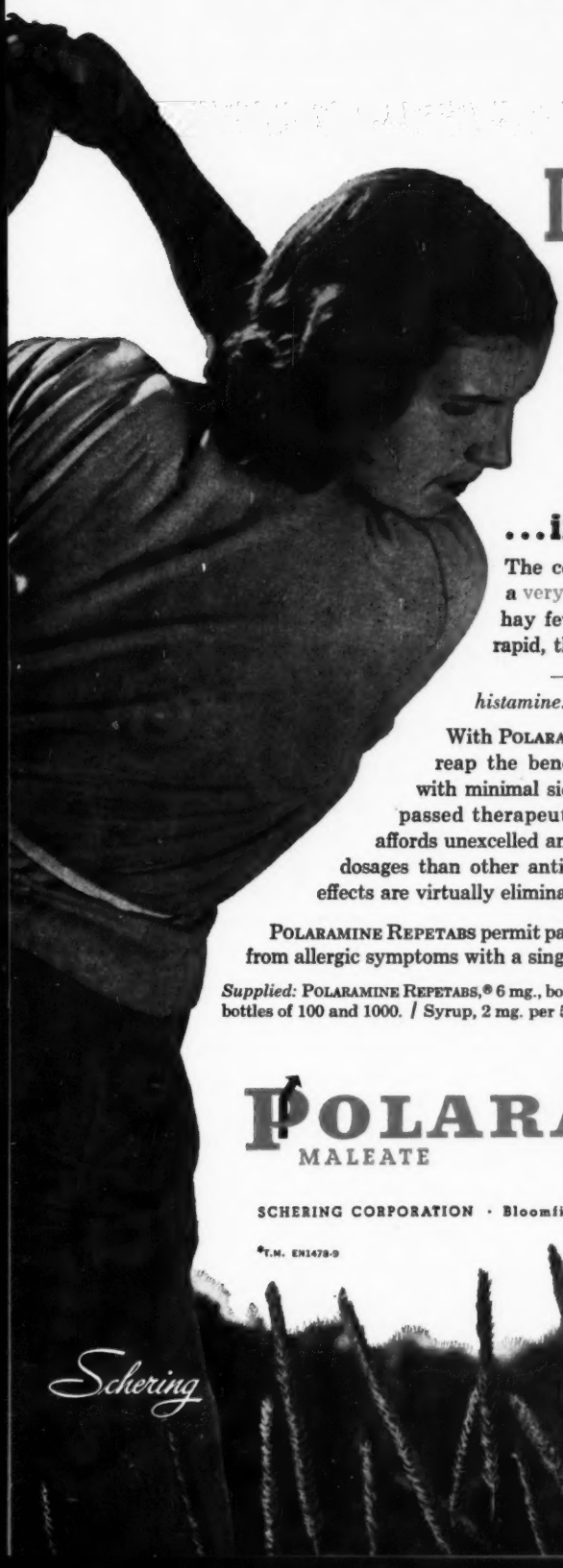
Oversized original illustrations should be photographed and a print on glossy paper submitted. Prints of a bluish tinge should be avoided. Large photomicrograph prints will be reduced in scale unless portions to be cropped are indicated by the author. The author should submit duplicate prints of roentgenograms and photomicrographs with the essential parts that are to be emphasized circled, as a guide to the photoengraver.

Charts and drawings should be in black ink on hard, white paper. Lettering should be large enough, uniform, and sharp enough to permit necessary reduction. Glossy prints of x-rays are requested. Paper clips should not be used on prints, since their mark shows in reproduction, as does writing on the back of prints with hard lead pencil or stiff pen. Labels should be prepared and pasted to the back of each illustration showing its number, the author's name, and an abbreviated title of the article, and plainly indicating the top. Charts and illustrations must have descriptive legends, grouped on a separate sheet. Tables must have captions. ILLUSTRATIONS SHOULD BE UNMOUNTED.

References to the literature should be limited to those used by the author in preparation of the article. They should be typed on a special page at the end of the manuscript. The citation should include, in the order given, name of author, title of article (with subtitle), name of periodical, with volume, page, month—day of month if weekly or biweekly—and year. References to books must contain, in the order given, name of author, title of book, city of publication, name of publisher, and year of publication.

AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street **Chicago 10**



DANGER IN THE ROUGH

...inviting pollenosis

The control of allergic symptoms is a very important problem for your hay fever patient. You can prescribe rapid, thorough relief with POLARAMINE —*close approach to a perfect antihistamine.*

With POLARAMINE your hay fever patient can reap the benefits of antihistamine therapy with minimal side effects. Because of its unsurpassed therapeutic effectiveness, POLARAMINE affords unexcelled antihistaminic protection at lower dosages than other antihistamines...and annoying side effects are virtually eliminated.

POLARAMINE REPETABS permit patients daylong or nightlong relief from allergic symptoms with a single medication.

Supplied: POLARAMINE REPETABS,® 6 mg., bottles of 100 and 1000. / Tablets, 2 mg., bottles of 100 and 1000. / Syrup, 2 mg. per 5 cc., bottles of 16 oz.

SYMBOL OF THE ONE-DOSE CONVENIENCE YOU WANT FOR YOUR PATIENT

PROMPT REPETAB RELIEF LASTS ALL DAY OR NIGHT

POLARAMINE* MALEATE

dextro-chlorpheniramine maleate

SCHERING CORPORATION · Bloomfield, New Jersey

*T.M. EN1478-9

Schering

There Is Nothing Like This on the Market Today!

X-RAY AND RADIUM IN DERMATOLOGY

By BERNARD A. WANSKER, M.D.

Charlotte, North Carolina. Formerly Instructor in Dermatology, Duke University School of Medicine; Diplomate, American Board of Dermatology, Durham, North Carolina

Those who are training in dermatology and those who use ionizing radiations will be equally interested in this **new** monograph. In a SHORT, CONCISE, UP-TO-DATE fashion Doctor Wansker has gathered widely scattered sources on roentgenology as it applies to the treatment of skin disorders. He has blended the material into a readily assimilated form.

WIDE IN SCOPE

- *PHYSICS OF RADIATION is presented without complicated calculus and formulae*
- *THE X-RAY CIRCUIT is fully discussed, adequately but simply illustrated*
- *PHYSICAL FACTORS affecting quality and quantity of x-irradiation are explained in detail*
- *FILTERED X-RAY TECHNIQUE AND LOW VOLTAGE (SUPERFICIAL) THERAPY are discussed*
- *SELECTED SPECIFIC METHODS OF THERAPY are presented in complete form*
- *INFORMATION ON CONTACT, GRENZ AND CATHODE RAYS is included*
- *USE OF RADIUM AND RADIOISOTOPES is presented from a theoretical and practical point of view*

"Evidence of a continuing desire on the part of practicing dermatologists to keep abreast and refreshed on this subject is attested to by the attendance of significant numbers of these physicians at the special course on x-ray and radium given at the American Academy of Dermatology and Syphilology meeting each year. In this day of confusing and conflicting information reaching the medical profession and the lay public, it behooves each of us who use ionizing radiations to refresh our minds on the fundamentals of their use."—*From the Introduction*

A Monograph in AMERICAN LECTURES IN DERMATOLOGY, edited by ARTHUR C. CURTIS, M.D., Chairman, Department of Dermatology and Syphilology, University of Michigan

Publication Date May 1959 **128 pages**
$5.00 **20 figures**

CHARLES C THOMAS • PUBLISHER

301-327 East Lawrence Avenue **Springfield • Illinois**

"severe decubitus ulcers... healed"*

*"...a paraplegic had severe decubitus ulcers [which had been resistant to previous treatment]. With PANAFIL ointment...the sacral decubitus ulcer was healed and there was marked improvement in the condition of the hip. ...No surgical intervention was necessary."—Burke, J. F., and Golden, T.: Am. J. Surg. 95:828, 1958.

panafil® topical enzyme therapy

Rystan
Mount Vernon, N.Y.

- effective wound cleansing and healing
- economical for hospital and patient
- well tolerated and convenient for outpatient use

PANAFIL Ointment (papain—urea—water-soluble chlorophyll derivatives). For complete information see your Physicians' Desk Reference.
32259

10 SPECIALTY JOURNALS

PUBLISHED MONTHLY
BY THE AMERICAN MEDICAL ASSOCIATION

NEUROLOGY

GENERAL PSYCHIATRY

SURGERY

PATHOLOGY

DISEASES OF CHILDREN

OPHTHALMOLOGY

INDUSTRIAL HEALTH

DERMATOLOGY

INTERNAL MEDICINE

OTOLARYNGOLOGY

Each journal offers the latest medical research and developments of outstanding specialists. Edited for the doctor by prominent authorities in each special field, these journals are of value not only to the specialist but to the general practitioner as well.

To order your subscription to one of the A.M.A.'s specialty journals use the form below.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn • Chicago 10

Please enter my subscription to the specialty journal checked at right.
Remittance for ☐ one year ☐ two years is enclosed.

NAME_____

ADDRESS_____

CITY_____ ZONE____ STATE_____

(One year rates)	U.S.A. & Possessions APO's	Canada	Outside U.S.A. & Possessions
☐ A.M.A. Arch. Neurology	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Gen. Psychiatry	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Dermatology	12.00	12.50	13.50
☐ A.M.A. Arch. Industrial Health	10.00	10.50	11.50
☐ A.M.A. Arch. Internal Medicine	10.00	10.50	11.50
☐ A.M.A. Jrl. Diseases of Children	12.00	12.50	13.50
☐ A.M.A. Arch. Surgery	14.00	14.50	15.50
☐ A.M.A. Arch. Pathology	10.00	10.50	11.50
☐ A.M.A. Arch. Ophthalmology	12.00	12.50	13.50
☐ A.M.A. Arch. Otolaryngology	14.00	14.50	15.50

PRURITUS ANI

treated ORALLY with **Borcherdt's MALT SOUP EXTRACT (MALTSUPEX)** *shows good results*

We would like to send you the recently published paper by Dr. Louis H. Brooks who says, ***"It was found that administration of Malt Soup Extract in dosages of one or two tablespoonfuls twice daily produced favorable results. Within two or three days after beginning this simple regimen, the itching and burning usually disappeared. Frequently there was prompt remission of symptoms which was followed by improvement in the condition of the tissue of the anal canal and the perianal skin."****

What Malt Soup Extract is. It's a non-diastatic barley malt extract, neutralized with potassium carbonate.

How Malt Soup Extract works. It works by restoring the normal acid condition in the lower tract and by promoting the growth and development of aciduric bacteria.

How soon can results be expected? The itching and burning will usually disappear in about three days, while the healing of the perianal skin is usually complete in about three weeks.

What is the usual effective dose? Two tablespoonfuls, twice a day (heaping if powder) is the usual effective dose which can be reduced as symptoms disappear. (Allow for carbohydrate content when treating diabetics).

What forms are available? Two forms are to be found in most drug stores coast to coast—the original liquid and the newer, popular powder. Both are sold under the name: MALT SOUP EXTRACT (Maltsupex).

What sizes are to be had? Both powder and liquid come in 8 ounce and 16 ounce bottles.

**Diseases of the Colon & Rectum, Vol. 1, No. 5, Sept.-Oct. 1958*

Borcherdt Company

217 North Wolcott Avenue, Chicago 12, Illinois
In Canada, Chemo Drug Co., Ltd., Toronto, Canada

We will be glad to send you clinical samples of powder and (or) liquid.

Serving the Medical Profession
SINCE 1868

Borcherdt Company A
217 N. Wolcott Ave., Chicago 12, Ill.
Gentlemen: Please send me sample of Malt Soup Extract
☐ Powder ☐ Liquid and literature.

_____ M.D.

Address _____

City _____ Zone _____ State _____

A NEW WIDE-SPECTRUM TOPICAL MICROBICIDE

not an antibiotic . . . not a sulfonamide . . . not a nitrofuran

Triburon

& Triburon-HC

(containing hydrocortisone 0.5%)

EFFECTIVE EVEN AGAINST ANTIBIOTIC-RESISTANT STRAINS

HIGHLY ACTIVE

■ against most "pathogenic cocci [both staphylococci and streptococci] regardless of their resistance to antibiotics."[1]

■ against pathogens common in skin and wound infections.

VIRTUALLY NONSENSITIZING

■ in more than 4500 stringent, closed-patch sensitivity tests, the incidence of allergic response was less than 2 per cent.[2, 3]

■ in initial clinical studies, only 15 of 1014 patients developed evidence of skin irritation.

MINIMAL RESISTANT ORGANISMS

■ laboratory attempts to develop Triburon-resistant strains produced no substantial change in organism sensitivity.[1]

■ WIDE-SPECTRUM
■ RAPID-ACTING
■ WELL TOLERATED
■ NONSTAINING
■ ODORLESS

DIAGNOSIS AND NO. OF PATIENTS	DURATION OF TREATMENT	RESULTS	ADVERSE REACTIONS
Impetigo contagiosa (50)	Triburon 3-10 days	excellent	none
Ecthyma (24)	Triburon 5-14 days	excellent	none
Pustular folliculitis (16)	Triburon 1-3 weeks	infection controlled	3 complaints of burning
Dermatitis repens (18)	Triburon 1-2 weeks	infection controlled	none
Dermatitis repens (18)	Triburon-HC 1-4 weeks	excellent	none
Secondarily infected eczematous eruption (20)	Triburon 1-2 weeks	infection controlled	none
Secondarily infected eczematous eruption (64)	Triburon-HC 1-4 weeks	excellent	1 complaint of irritation

Chart based on finding of E. Edelson, E. Grunberg and T.V. Morton Jr.

PACKAGES:
Triburon Ointment, 1-oz tubes and 1-lb jars.
Triburon-HC Ointment, 5-Gm and 20-Gm tubes.

REFERENCES: 1. R. J. Schnitzer, E. Grunberg, W. F. DeLorenzo and R. E. Bagdon, to be published.
2. E. Edelson, E. Grunberg and T. V. Morton, Jr., Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959.
3. R. C. V. Robinson and L. E. Harmon, Antibiotics Annual 1958-1959.

TRIBURON™· triclobisonium chloride — N,N'-bis[1-methyl-3-(2,2,6-trimethylcyclohexyl) propyl]-N,-N'-dimethyl-1,6-hexanediamine bis (methochloride). ROCHE®

ROCHE LABORATORIES • Division of Hoffmann-La Roche Inc • Nutley 10 • New Jersey

FRIGIDERM®

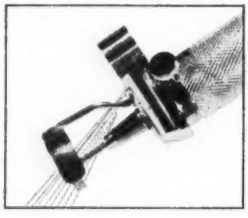
(100% dichloro-tetrafluoro-ethane...contains no ethyl-chloride)

SKIN REFRIGERANT–ANESTHETIC

*Widely Accepted for Local Anesthesia in Surgical Planing of the Skin**

JET-SPRAY PLANER

This hand-tooled, precision-built instrument with diamond fraises is available for most standard planing units. In ordering, please specify make of planing unit. Full information on request.



FRIGIDERM has been researched and developed to meet the expressed need of physicians for a well tolerated skin refrigerant-anesthetic...non-explosive, non-inflammable...having no general anesthetic properties.

Today, **FRIGIDERM** is one of the preferred products of its kind among Dermatologists everywhere.

FRIGIDERM quickly produces local anesthesia for surgical planing in the treatment of scarring due to acne, chickenpox, smallpox and trauma...multiple senile keratoses...fine wrinkling...traumatic tattoos.

Also for incision of furuncles, electrocautery to small cutaneous tags, flat warts, or for alleviation of needle pain during hypodermic injection.

This freezing agent can be delivered from the spray-top container shown above by easy finger pressure.

Now in the improved 8 oz. container — $2.00

Fully guaranteed for satisfactory performance
Available at your surgical supply dealer

**A.M.A. Archives of Dermatology, April 1955*
Ref.: Wilson, J. W.; Luikart II, R.; Ayres III, S., Reprints available

® REGISTERED TRADE MARK

W. T. BRACHVOGEL

1723 WEST SEVENTH STREET • DUNKIRK 4-9273 • LOS ANGELES 17, CALIFORNIA

three-way comparative study demonstrates "full-healing effect" of HYDRO-TAR™ in acute & chronic dermatoses

(Liquor Carbonis Detergens with Hydrocortisone, Almay)

A CASE IN POINT—ATOPIC DERMATITIS OF BOTH HANDS

1. Hydrocortisone alone suppresses inflammation. 2. Coal tar alone corrects eczematous manifestations. 3. Both agents combined in HYDRO-TAR speed complete early healing. Mutually supportive action produces the "full-healing" effect. Presence of hydrocortisone permits well-tolerated coal-tar therapy even during the acute phases of severe dermatoses.

Dosage: **Apply by gentle massage to affected areas 3 or 4 times a day; 0.5% for moderately severe dermatoses or maintenance – 1.0% for severe dermatoses.**

Supplied: **15 Gm. tubes in 0.5% and 1.0% strengths. Samples and literature sent on request.**

ALMAY Division of *Schieffelin & Co. / Since 1794*
Pharmaceutical Laboratories Division, New York 3, New York

Schieffelin 17 94 Quality Integrity Service

AVAILABLE SOON

THE FIRST ORALLY EFFECTIVE TRE

GRiFUL

Griseofulvin

"...AN ADVANCE IN THE TREATMENT OF SUPERFICIAL FUNGOUS INFECTIONS COMPARABLE TO PENICILLIN IN BACTERIAL INFECTIONS."

—Wrong, N. M.: Canad. M.A.J. **80**:656 (April 15) 1959.

TMENT FOR RINGWORM INFECTIONS

VIN*

IN FUNGOUS INFECTIONS OF THE SKIN, HAIR AND NAILS

- Tinea corporis usually clears in 2 to 4 weeks; itching stops in 3 to 5 days.
- Tinea pedis improves in 1 to 2 weeks but may require 3 to 6 weeks to clear.
- Tinea capitis improves in 2 to 3 weeks and is usually cured in 3 to 5 weeks.
- Onychomycosis (ringworm of the nails) takes at least 3 to 4 months to clear, but new normal growth is seen earlier.

GRIFULVIN will be available soon as 250 mg. scored tablets, colored aquamarine, imprinted McNEIL, in bottles of 16.

*Trade-mark

McNEIL

McNEIL LABORATORIES, INC • PHILADELPHIA 32, PA.

"ulcers were cleaned up promptly"*

*"....previously treated unsuccessfully with antibiotic or antibacterial ointments... the ulcers were cleaned up promptly and complete healing was obtained.... Necrotic tissue was effectively dissolved without injury to the viable tissues.... Local infection was uniformly eradicated...." —Carter, C. H.: M. Times 86:1382 (Nov.) 1958.

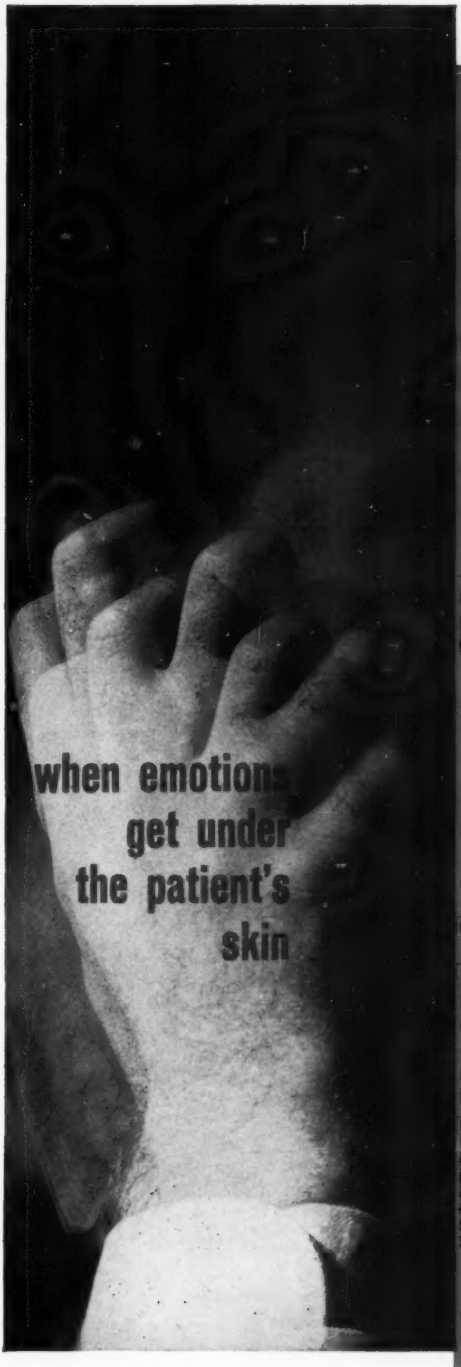
panafil®
topical enzyme therapy

Rystan
Mount Vernon, N.Y.

- effective wound cleansing and healing
- well tolerated and convenient for outpatient use
- economical for hospital and patient

PANAFIL ointment (papain–urea–water-soluble chlorophyll derivatives) • For complete information see your Physicians' Desk Reference

32559



A TRANQUILIZER UNIQUE
IN DERMATOLOGIC PRACTICE

dermatoses respond to

the calming action

Feinberg: "Tranquilizing drugs in general have an equivocal effect on the manifestations of allergic disease. . . . ATARAX may be one exception to the rule. . . ."[1]

and the anti-allergic effect

—Added antihistaminic action of ATARAX controls a wide variety of dermatological exacerbations: pruritus, urticaria, dermatitis, and other cutaneous eruptions.[2,3,4,5]

# of ATARAX®

(brand of hydroxyzine)

Feinberg[1] obtained "most striking results" in 17 patients with chronic urticaria. The effect of ATARAX was excellent in 15, fair to good in 2. After objective evaluation of 140 patients, Robinson[5] concludes that ATARAX is "valuable adjunctive therapy" for patients whose dermatoses are related to emotional tension.

Dosage: Adults, one 25 mg. tablet, or one tbsp. Syrup q.i.d. Children, 1 or 2 tsp. Syrup t.i.d.

Supplied: Tiny 10 mg., 25 mg., and 100 mg. tablets, bottles of 100. Syrup, pint bottles. Parenteral Solution, 10 cc. multiple-dose vials.

References: 1. Feinberg, A. R., et al.: J. Allergy 29:354 (July) 1958. 2. Robinson, H. M., Jr., et al.: South. M. J. 50:1282 (Oct.) 1957. 3. Santos, I. M., and Unger, L.: Paper presented at 14th Annual Congress, American College of Allergists, Atlantic City, New Jersey, April 23-25, 1958. 4. Coirault, M., et al.: Presse méd. 64:2239 (Dec. 25) 1956. 5. Robinson, H. J., Jr., et al.: J.A.M.A. 161:604 (June 16) 1956.

Rx PFIZER

New York 17, N. Y.
Division, Chas. Pfizer & Co., Inc.
Science for the World's Well-Being

The
1-2-3 Treatment
for
Warm Weather Dermatoses

Poison ivy, poison oak, insect bites, Anogenital eczema, athlete's foot, superficial mycoses, Acute and subacute contact and allergic dermatitis.

Samples and literature on request

1 ACUTE STAGE
DOMEBORO® pH 4.2
Cool Wet Dressings

2 POST TREATMENT
ACID MANTLE®
Creme pH 4.2 • Lotion pH 4.5

3 FOR DESTROYING FUNGI
QUATRASAL®
Fungicidal Spray

DOME Chemicals Inc.
NEW YORK 23 • LOS ANGELES 46 • In Canada: 2765 Bates Rd., Montreal
THE MOST TRUSTED NAME IN DERMATOLOGICALS

1. DOMEBORO (Burow's Solution)
2. ACID MANTLE (aluminum acetate in specially formulated bases)
3. QUATRASAL (salicylanilide, trimethyl octadecyl ammonium pentachlorophenate, and isopropl alcohol 94%)

Pleasingly and efficiently
serving patient and physician
during all seasons

SUPERFATTED

BASIS® SOAP

For dry sensitive skin

Available at Prescription Pharmacies

DUKE LABORATORIES, INC.
SOUTH NORWALK, CONN., U. S. A.

Mfrs. of Aquaphor®—Elastoplast®

in urticaria and pruritus

VISTARIL* provides:

hydroxyzine pamoate

SPECIFIC ANTIHISTAMINIC EFFECT

in the treatment of a variety of skin disorders commonly seen in your practice.

"The most striking results were seen in those patients with chronic urticaria of undetermined etiology."[1]

. . . reduces—erythema, excoriation, and extent of lesions.[1-4]

PSYCHOTHERAPEUTIC POTENCY

for effective relief of tension and anxiety.[1-4]

Recommended Oral Dosage: 50 mg. q.i.d. initially; increase or decrease according to individual response.

Supplied as: Vistaril Capsules—25 mg., 50 mg. and 100 mg.

Vistaril Parenteral Solution—10 cc. vials and 2 cc. Steraject® Cartridges, each cc. contains 25 mg. hydroxyzine (as the HCl).

*Trademark

More than a tranquilizer

Pfizer *Science for the world's well-being*

PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, New York

References: 1. Feinberg, A. R., et al.: J. Allergy *29*:358 (July) 1958. 2. Eisenberg, B. C.: Clin. Med. *5*:897-904 (July) 1958. 3. Robinson, H. M., Jr., et al.: J.A.M.A. *161*:604-606 (June 16) 1956. 4. Robinson, H. M., Jr., et al.: South. M. J. *50*:1282 (Oct.) 1957.

now–
the unsurpassed advantages of Aristocort
in
topical form

Aristo

equivalent potency of hydrocortisone topically
with only one-tenth of the steroid required.
This means you can prescribe

unsurpassed
topical therapy...
for
more patients...
with
great security

Lederle LEDERLE LABORATORIES

For the great variety of inflammatory skin conditions seen daily in office and clinic

ARISTOCORT CREAM is highly effective on application of only very small quantities to affected areas. This new form of ARISTOCORT is more potent than conventional corticosteroids (studies show it to have 10 times the potency of hydrocortisone). Yet ARISTOCORT CREAM *does not cause sodium and water retention, rarely causes sensitization* or *irritation,* and is *cosmetically acceptable.*

cort®

CREAM

Triamcinolone Acetonide 0.1% LEDERLE

PATIENTS PREFER ARISTOCORT CREAM

Blau and Kanof[1] found that of 21 patients with pruritic dermatoses treated with ARISTOCORT CREAM, 19 showed "good" to "marked" improvement. In paired comparison studies, 7 of 11 patients responded better to ARISTOCORT CREAM 0.1% than to hydrocortisone cream 1%, while 4 showed equal improvement with these two preparations. There was no primary irritation or allergic sensitization with ARISTOCORT CREAM.

Orentreich[2] made a double-blind study of 71 patients with a variety of dermatoses treated with ARISTOCORT CREAM 0.1% and 1% hydrocortisone acetate cream. Twenty-eight per cent of the patients preferred ARISTOCORT CREAM to the hydrocortisone cream, 68% found both creams equally effective, while only 4% preferred hydrocortisone.

Callaway[3], in a comparison study of 62 patients with various dermatoses treated with ARISTOCORT CREAM and hydrocortisone, concluded that ARISTOCORT CREAM 0.1% is as effective as 1% hydrocortisone in comparable conditions. "In no instance have we seen any evidence of sensitization develop and in no patient has there been any evidence of primary irritation." He describes ARISTOCORT CREAM as "a welcome addition to our dermatological armamentarium."

Robinson[4] also reported that 0.1% triamcinolone acetonide in a water-miscible base was at least as effective as 1% hydrocortisone in an identical base. He found it significant that of 40 patients in this comparison study, 12 preferred triamcinolone acetonide to hydrocortisone while only 3 preferred hydrocortisone.

Indications: atopic dermatitis, eczematous dermatitis, nummular eczema, contact dermatitis, pruritus vulvae and ani, generalized erythrodermia, external otitis, seborrheic dermatitis, eczematized psoriasis, neurodermatitis, eczematized mycotic dermatitis.

Dosage: ARISTOCORT CREAM should be applied in small quantities to the affected areas three or four times daily.

ARISTOCORT CREAM contains: Triamcinolone acetonide 0.1% as the active ingredient; 0.16% methylparaben and 0.04% propylparaben as preservatives; and, in a water base, glyceryl monostearate, squalene, polysorbate 80, spermaceti, stearyl alcohol and sorbitol.

Supply: 5 Gm. and 15 Gm. tubes.

References: 1. Blau, S., and Kanof, N. B.: Clinical Report, cited by permission. 2. Orentreich, N.: Clinical Report, cited by permission. 3. Callaway, J. L.: Clinical Report, cited by permission. 4. Robinson, R. C. V.: *Bull. School Med. Univ. Maryland,* 43:54, July, 1958.

A Division of AMERICAN CYANAMID COMPANY • Pearl River, New York

these physical scars need never have developed

Surgical techniques can now almost completely remove this man's severe acne scars. But if he, and thousands like him, had sought early treatment, the scars might never have developed. A physician's advice and guidance concerning his condition, plus treatment with 'Acnomel', might have prevented his acne from progressing to the severe, scarring stage.

'Acnomel' conceals acne lesions as it heals them, thus reducing embarrassment while treatment goes on. The results from 'Acnomel' therapy are often evident in a few days rather than in weeks or months.

When you see a patient who needs advice about acne, remember 'Acnomel'. Available in 2 forms: Cream for use at home; Cake in a handy compact for use away from home.

Acnomel* sulfur • resorcinol • hexachlorophene **conceals as it heals**

Smith Kline & French Laboratories, Philadelphia *T.M. Reg. U.S. Pat. Off.

The improved, new local anesthetic. What's the new, highly efficient local anesthetic for minor surgical procedures? Many physicians say it's Gebauer's new Fluro-Ethyl. An actual report: "I have used your mixture of 25% Ethyl Chloride and 75% "Freon" for skin planing and I find it most efficient for my purposes. Freezing is fast, each container lasts a long time, results are highly satisfactory".

Equally useful as a local anesthetic for incision of furuncles, electrocautery to small cutaneous tags, flat warts, nevi, and alleviation of needle pain in hypodermic injection. Non-flammable, requires no blower. Compare Fluro-Ethyl with the product you have been using. Gebauer Chemical Company, 9410 St. Catherine Avenue, Cleveland 4, Ohio.

① Gebauer's Ethyl Chloride in new Dispensaal amber glass. ② Metal tube for doctor's emergency kit. ③ Fluro-Ethyl in the aerosol container.

FLURO-ETHYL
GEBAUER
CHEMICAL COMPANY

'B. W. & CO.'® ANTIBIOTIC LOTIONS FOR TOPICAL BACTERIAL INFECTIONS

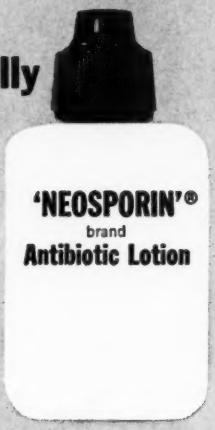
Antibiotics

- Of proven effectiveness
- That rarely sensitize
- To which resistance or cross-resistance rarely develops clinically
- That are seldom used systemically

NEW

BACTERICIDAL
ANTI-INFLAMMATORY

Each cc. contains:
'Aerosporin'®
brand Polymyxin B Sulfate
10,000 Units
Neomycin Sulfate...5 mg.
Hydrocortisone...(1%)10 mg.
in a special
water-miscible lotion
base. Plastic squeeze
bottles of 10 cc.

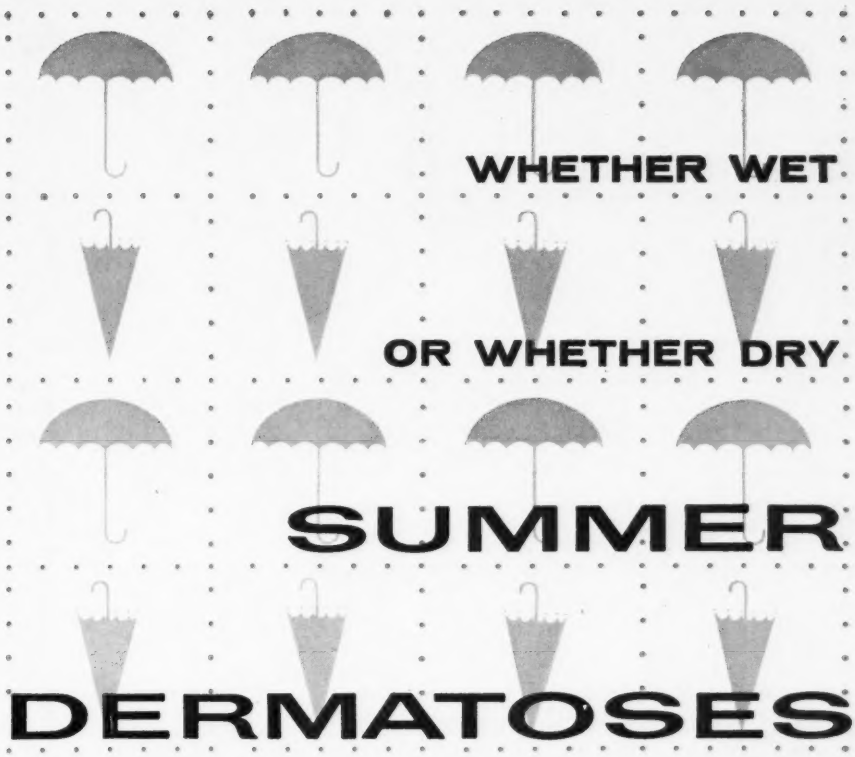


BACTERICIDAL

Each cc. contains:
'Aerosporin'®
brand Polymyxin B Sulfate
10,000 Units
Neomycin Sulfate...5 mg.
in a special
water-miscible lotion
base. Plastic squeeze
bottles of 20 cc.

The assurance of proven formulas—
"Cosmetically acceptable"
to the patient

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York



such as poison ivy, sunburn and prickly heat promptly respond to soothing

AVEENO® Colloid Baths

if it's wet...

℞ **AVEENO Colloidal Oatmeal**

reduces inflammation... relieves pruritus... mildly drying for wet dermatoses

AVEENO Colloidal Oatmeal is available in 18 oz. and 4 lb. boxes.

if it's dry...

℞ **AVEENO "OILATED"**

(soothing colloidal oatmeal plus *35% emollient oils)*

lubricates the skin... softens dry, crusting lesions

AVEENO® "OILATED" colloidal oatmeal is available in 10 oz. cans.

AVEENO CORPORATION 250 West 57th Street New York 19, N. Y.

Pioneers in Ethically Promoted Colloid Baths

Incorporated in exclusive ACID MANTLE vehicle

Quick Soothing Topical Response

IN INFLAMMATORY DERMATOSES

Cort-Dome™

Acid Mantle-Hydrocortisone

CREME AND LOTION—pH 4.6

ABATES INFLAMMATION AND RESTORES NORMAL SKIN ACIDITY

"Susceptibility to infection by bacteria is widely held to be due to the removal of the antibacterial 'acid mantle' of the skin and its displacement by an abnormal 'alkaline mantle'."—Fabricant, N. D.: A. M. A. Arch. Otolaryn. 65:11, 1957.

Supply—½%, 1% and 2% hydrocortisone in either Creme (½ oz., 1 oz., 2 oz., 4 oz. tubes and 1 lb. jars) or Lotion (½ oz., 1 oz., 2 oz., 4 oz. squeeze bottles and pt. bottles).

Samples and literature available on request.

Dome Chemicals Inc.

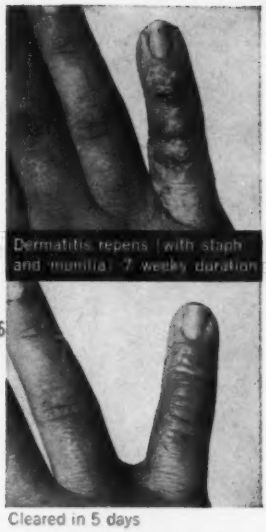
NEW YORK 23 • LOS ANGELES 46 • In Canada: 2765 Bates Road, Montreal

new for total management of itching,[1,2] inflamed,[3,4] infected[5,6] skin lesions

Mycolog ointment

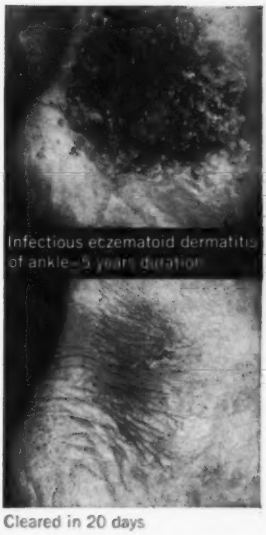
Kenalog, Spectrocin and Mycostatin in Plastibase

antipruritic/anti-inflammatory/antibacterial/antifungal



Dermatitis repens (with staph and monilia) 7 weeks duration

Cleared in 5 days



Infectious eczematoid dermatitis of ankle—5 years duration

Cleared in 20 days

Mycolog Ointment – containing a new superior topical corticoid Kenalog – reduces inflammation,[3,4] relieves itching,[1,2] and combats or prevents bacterial, monilial and mixed infections.[5-7] It is extremely well tolerated, and assures a rapid, decisive clinical response for most infected dermatoses.

> **"Thirty-one of 38 patients . . . obtained excellent or good control of dermatological lesions . . . [Mycolog] was highly effective, particularly in the management of mixed infections. Several recalcitrant eruptions which had not responded to previous therapy were remarkably responsive to the daily application of this preparation over periods of 2 to 3 weeks."[5]**

For total management of itching, inflamed, infected skin lesions, Mycolog contains triamcinolone acetonide, an outstanding new topical corticoid for prompt, effective relief of itching, burning and inflammation[1-4] – neomycin and gramicidin for powerful antibacterial action[7] – and nystatin for treating or preventing Candida (Monilia) albicans infections.[8,9]

Application: Apply 2 to 3 times daily. Supply: 5 Gm. and 15 Gm. tubes. Each gram supplies 1.0 mg. (0.1%) triamcinolone acetonide, 2.5 mg. neomycin base, 0.25 mg. gramicidin, and 100,000 units nystatin in PLASTIBASE.

References: 1. Shelmire, J.B., Jr.: Monographs on Therapy 3:164 (Nov.) 1958. - 2. Nix, T.E., Jr., and Derbes, V.J.: Monographs on Therapy 3:123 (Nov.) 1958. - 3. Robinson, R.C.V.: Bull. School of Med., U. Maryland 43:54 (July) 1958. - 4. Sternberg, T.H., Newcomer, V.D., and Reisner, R.M.: Monographs on Therapy 3:115 (Nov.) 1958. - 5. Clark, R.F., and Hallett, J.J.: Monographs on Therapy, 3:153 (Nov.) 1958. - 6. Smith J.G., Jr., Zawisza, R.J., and Blank, H.: Monographs on Therapy, 3:111 (Nov.) 1958. - 7. Monographs on Therapy, 3:137 (Nov.) 1958. - 8. Howell, C.M., Jr.: North Carolina M.J. 19:449 (Oct.) 1958. - 9. Bereston, E.S.: South. M.J. 50:547 (April) 1957.

And whatever the topical corticoid need, a suitable Squibb formulation is available—Kenalog-S Lotion—7½ cc. plastic squeeze bottles. Each cc. supplies 1.0 mg. (0.1%) triamcinolone acetonide, 2.5 mg. neomycin base and 0.25 mg. gramicidin. Kenalog Cream, 0.1%—5 Gm. and 15 Gm. tubes. Kenalog Lotion, 0.1%—15 cc. plastic squeeze bottles. Kenalog Ointment, 0.1%—5 Gm. and 15 Gm. tubes.

RELIABILITY INTEGRITY SERVICE

SQUIBB

Squibb Quality — the Priceless Ingredient

"SPECTROCIN"®, "MYCOSTATIN"®, "PLASTIBASE"®, "MYCOLOG" AND "KENALOG" ARE SQUIBB TRADEMARKS

stop penicillin reactions

before they become serious

NEUTRAPEN®

(NEUTRAlizes PENicillin) (Penicillinase Injectable,* SchenLabs)

the only specific for penicillin reactions

"... if every patient with a penicillin reaction were given penicillinase [NEUTRAPEN] *within 24 to 48 hours ... I do not think we would see the severe, prolonged reactions we are seeing now."*

R. M. Becker, Antibiotics Annual 1957-58.[1]

Unlike the antihistamines, ACTH or steroids which treat effects, NEUTRAPEN, an enzyme, aborts penicillin reactions by counteracting their cause—it destroys the penicillin itself and is effective in about 97 per cent of cases.[2] Over 80 per cent of patients obtain clearing of the reaction with one injection.[3]

Obscure sources—even cases with no history of penicillin therapy respond to NEUTRAPEN when the reaction has been caused by penicillin from such sources as milk, Roquefort or bleu cheese, or penicillin containing vaccines.[3]

NEUTRAPEN—800,000 units I.M.—should be given as soon as symptoms appear. May be repeated on the third day if response is not satisfactory. In anaphylactic reactions, after routine emergency measures—800,000 units intravenously, followed immediately by 800,000 units intramuscularly.
contraindications: None. *side effects:* Occasionally transient local soreness, erythema, and edema; rarely, transitory chills and fever.
supplied: 800,000-unit single-dose vials of lyophilized penicillinase powder. Stable at room temperature in the dry state.
references: (1) Becker, R. M., in Welch, H., and Marti-Ibañez, F.: Antibiotics Annual 1957-1958, New York, Medical Encyclopedia, Inc., 1958, p. 310. (2) Zimmerman, M. C.: Clin. Med. *5*:305, 1958. (3) Zimmerman, M. C.: J.A.M.A. *167*:1807, 1958.

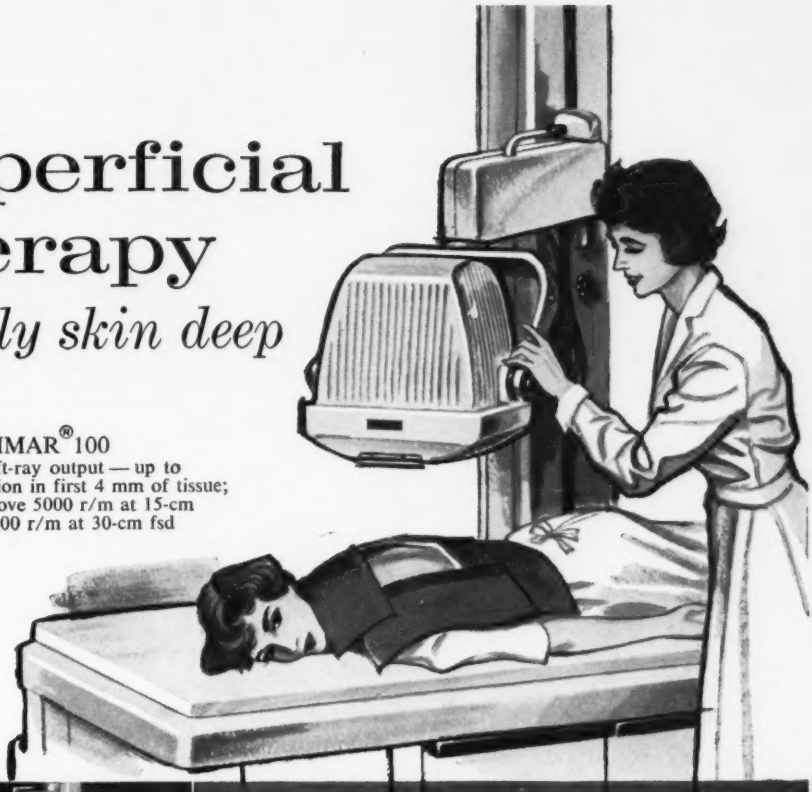
®T. M. REG. U.S. PAT. OFF. *PATENTS PENDING. 55658

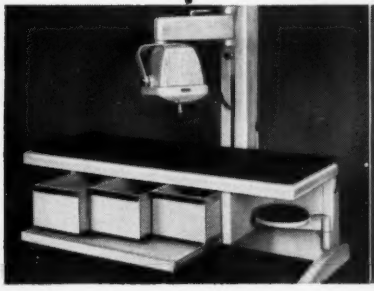
SchenLabs SCHENLABS PHARMACEUTICALS, INC • NEW YORK 1, N.Y.

superficial therapy

...*truly skin deep*

G-E MAXIMAR®100
multiplies soft-ray output — up to 84% absorption in first 4 mm of tissue; dose rates above 5000 r/m at 15-cm fsd, above 1200 r/m at 30-cm fsd





ARM'S-REACH CONVENIENCE FOR EVERYTHING YOU NEED...

Comfortably cushioned table — includes swing-out treatment seat . . . drawer for *flat storage* of lead-rubber sheeting . . . bins for all accessories.

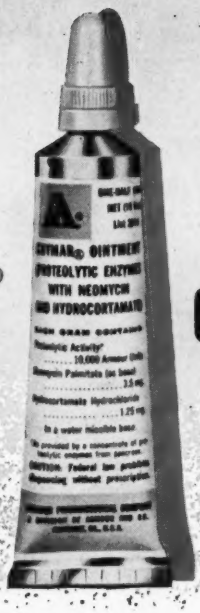
Those times when *skin deep* is exactly *deep enough* — that's when you'll truly appreciate your Maximar 100. Foremost reason is its exclusive Coolidge tube with beryllium window: soft rays exit *in quantity* — are not filtered out as they would be with other materials. So Maximar 100's range easily extends from output approaching grenz rays to the depth penetration obtained at 100 kvp. Control is precise . . . dosage exact. And coverage at 30-cm focal/skin distance will span at least an 18-cm circle — perimeter output remaining at least at 80% of full center strength on an 18-cm circle! Talk over details of the Maximar 100 soon with your G-E x-ray representative. Or write X-Ray Department, General Electric Company, Milwaukee 1, Wisconsin, for illustrated Pub. P-72.

Progress Is Our Most Important Product

GENERAL ELECTRIC

Announcing

CHYMAR® OINTMENT



combining proteolytic, antibiotic, corticoid activity

CLEANS the wound

- removes necrotic tissue, crusted cell debris, pyogenic membrane, exudates
- exposes wound surface to full effects of the anti-infective and anti-inflammatory agents

CLEARS infection

- destroys both gram-negative and gram-positive bacteria
- prevents further bacterial invasion

CONTROLS inflammation

- reduces topical erythema, edema and pruritus

Each gram of Chymar Ointment contains:
Proteolytic Activity*...10,000 Armour Units
Neomycin Palmitate (as base).....3.5 mg.
Hydrocortamate Hydrochloride....1.25 mg.
In a water-miscible base.

*Provided by a concentrate of the pancreatic enzymes (e.g. chymotrypsin and trypsin).

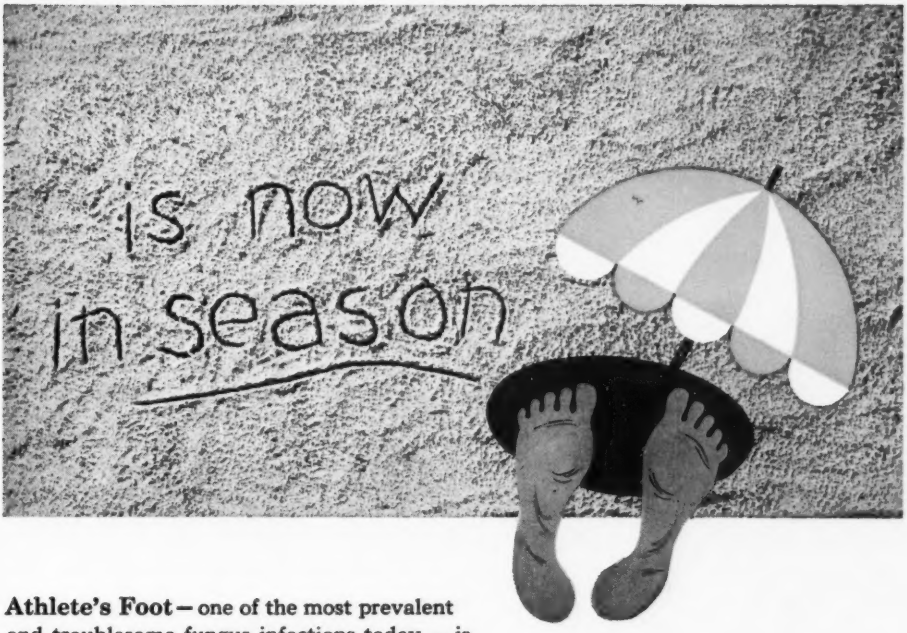
The extremely high water solubility of the corticoid assures maximum penetration. The water-miscible ointment base permits fullest release of the medicaments for fullest therapeutic benefit. Systemic effects do not occur; hypersensitivity reactions are uncommon.

Chymar Ointment is available in 1/6 oz. (5 Gm.) and 1/2 oz. (15 Gm.) tubes.

ARMOUR PHARMACEUTICAL COMPANY • KANKAKEE, ILLINOIS
ARMOUR *A Leader in Biochemical Research*

contact dermatitis • infectious dermatitis • seborrheic dermatitis • stasis dermatitis • neurodermatitis (infected) • burns • cuts and abrasions • boils • psoriasis • impetigo • ulcers • eczema

athlete's foot



Athlete's Foot – one of the most prevalent and troublesome fungus infections today – is estimated to affect 90% of the population at one time or another. Desenex, containing the unsaturated fatty acid, undecylenic acid, has proved to be one of the most potent antimycotic agents known for effective treatment of superficial fungus infections.

Night and Day Treatment
At Night – Desenex Ointment (zincundecate) – 1 oz. tubes. **During the Day** – Desenex Powder (zincundecate) – 1½ oz. container. Also – Desenex Solution (undecylenic acid) – 2 fl. oz. bottles. In Otomycosis – Desenex Solution or Ointment.

Maltbie **Write for samples**

MALTBIE LABORATORIES DIVISION
Wallace & Tiernan Inc. • Belleville 9, N. J.

Desenex®
FOR ATHLETE'S FOOT

fast relief from itching
prompt antimycotic action
continuing prophylaxis

PD-92

Most of your patients spend many hours in the sun during the summer months — working and playing. To help you help them enjoy freedom from uncomfortable, dangerous sunburning, the Texas Pharmacal Company offers a selection of sun protective products for every skin type.

Å-Fil® Sun Stick

contains digalloyl trioleate in a colorless, emollient base — to keep lips soft and smooth — and free from painful sunburn and windburn. Easily applied with the handy new swivel type case. Ideal for skiing, fishing, any outdoor activity.

Å-Fil® Sun Protective Cream

contains menthyl anthranilate and titanium dioxide in a tinted, vanishing cream type base to prevent sunburning **and** suntanning through complete chemical and physical protection. Especially suitable for mountain sports and extra long hours on the golf course, on the water, on the job.

Neo Å-Fil®

contains digalloyl trioleate in a colorless, emollient, vanishing cream type base. Prevents sunburning, but promotes suntanning. For individuals wanting something to show for the hours spent in the sun.

Allercreme® Saf-Tan® Cream

beautifully-decorated "cosmetic" package of Neo A-Fil, slightly more perfumed, particularly appealing to women.

For further details or a complimentary stock size package of any Å-Fil sun product for your personal sun protection, write . . .

IN CANADA—Omega Laboratories, Ltd., Montreal and Toronto
IN VENEZUELA—Salus, C. A., Caracas

TEXAS PHARMACAL COMPANY
San Antonio, Texas

For acne and pimples with extensive flush areas

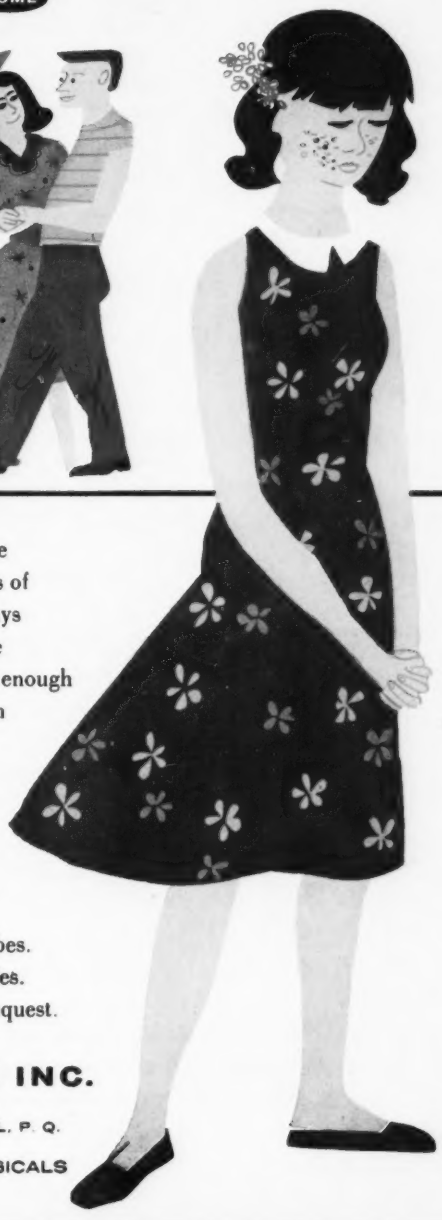
Acne Cort-Dome™

Hydrocortisone with sulfur, bithionol, resorcinol monacetate, in aluminum acetate vehicle pH 5.0

CREME or LOTION

DOME

antiinflammatory/keratolytic



INCORPORATED IN EXCLUSIVE ACID MANTLE VEHICLE ®

Within a short period of time suppresses the epidermatitis of acne, reduces erythema, allays inflammation, soothes acute exacerbations and produces enough peeling action to gently open the papules and pustules. Restores and maintains normal acidity of the skin.

SIG: Apply morning and night to skin after washing and at night to scalp.

SUPPLY: Creme in 1 oz. tubes. Lotion in 1 oz. squeeze bottles. Samples and literature on request.

DOME CHEMICALS INC.

NEW YORK 23 LOS ANGELES 46

IN CANADA: 2765 BATES RD., MONTREAL, P. Q.

A TRUSTED NAME IN DERMATOLOGICALS

No longer *itched*

bothered or

bewildered

Pruritus is relieved rapidly and erythema and lichenification of the skin are reduced within a short period after initial application of NEO-CORT-DOME. Secondary infection is controlled and the normal pH of the skin and external auditory canal is restored and maintained with NEO-CORT-DOME.

FOR INFECTIOUS DERMATOSES AND OTITIS EXTERNA

NEO-CORT-DOME™

CREME AND LOTION pH 4.6

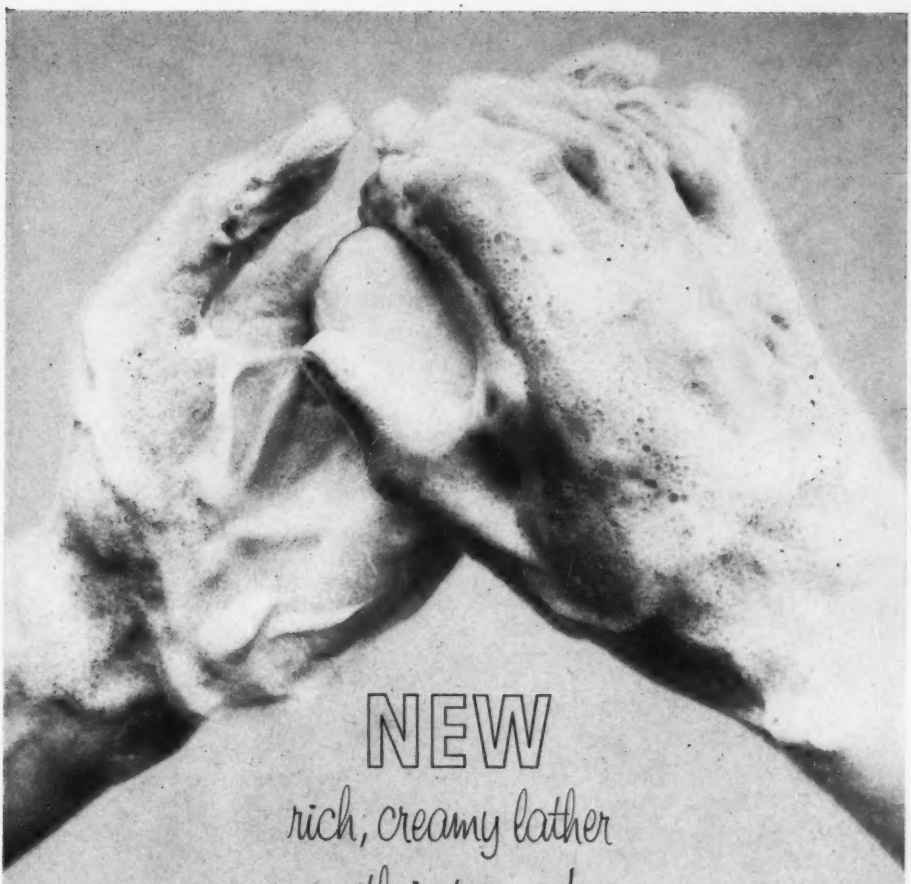
DOME

Hydrocortisone—Neomycin—In Aluminum Acetate Vehicle

Note: Lotion is especially effective in hairy areas and in tissue folds. *Supply:* ½% or 1% hydrocortisone, with 5 mg. per gm. Neomycin Sulfate in ½ oz., 1 oz., 4 oz. squeeze bottles. (½ oz. size has special soft plastic tip for easy application into external ear in otitis externa). *Sample* and literature available on request.

INCORPORATED IN EXCLUSIVE ACID MANTLE VEHICLE

DOME CHEMICALS INC.
125 West End Avenue, New York 23
665 N. Robertson Blvd., Los Angeles 46
In Canada: 2675 Bates Road, Montreal



NEW

rich, creamy lather
with improved

LOWILA® CAKE

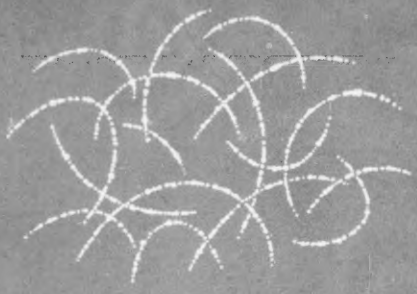
NEW . . . because Lowila* Cake has undergone a change. It now provides a rich, creamy, more abundant lather and has a smoother feel.

Lowila Cake cleans tender or dermatitic skin with virtually no irritation. It maintains the skin's normal acid lipid film and creates an environment favorable to therapy and healing.

*Contains sodium lauryl sulfoacetate in a corn dextrin base, acidified with lactic acid.

In bar form. Write for samples.

WESTWOOD PHARMACEUTICALS
BUFFALO 13, NEW YORK



Used in every type of practice and clinical specialty today, EQUANIL® (meprobamate, Wyeth) has proved that anxiety and tension *can* be controlled to smooth the course of diagnosis, treatment, and convalescence. Anxiety is a fact of life. Anxiety is a fact of illness.

Wyeth
Philadelphia 1, Pa.

A.M.A. ARCHIVES OF
DERMATOLOGY

The Changing Pattern of Dermatology

G. A. GRANT PETERKIN, M.B.E., M.B., F.R.C.P.Ed., Edinburgh, Scotland

Mr. President, Ladies, and Gentlemen:

To this meeting of the American Academy of Dermatology I should like to express my most sincere and profound thanks for your kind invitation to this conference and for the signal honor you have bestowed on me in asking me to speak this afternoon and in so speaking to pay tribute to the late James Webster, your deceased President, whose name is thus commemorated. I had not the pleasure of knowing Jim Webster as you did, but his character can be summed up in the words of one of your most distinguished dermatologists: "He was a fine person, kindly, tolerant and well mannered. He was one of the people that everyone liked and he was always a credit to Dermatology."

He loved the Academy and the Academy loved him. In fact, he might be said to have devoted his life to the Academy.

An old Chinese sage said that there are only two forms of immortality—"one is to be a teacher and the other is to have children." What better teaching could there be than this Academy? And what is finer than to have had a devoted wife and to have two sons inspired to follow the long line of Websters in medicine? "Si monumentum requiris, circumspice."

Submitted for publication Jan. 21, 1959.

Physician-in-Charge, Skin Department, Royal Infirmary.

A portion of this address appeared in *The Medical Press* 238:311, 1957.

The First James R. Webster Memorial Lecture, delivered on Dec. 7, 1958, at the American Academy of Dermatology & Syphilology, Chicago.

As my subject this afternoon, I have selected a wide and general topic which I have called "The Changing Pattern of Dermatology," as I have seen it unfolded over the past 25 years; I intend to refer particularly to the ways in which cutaneous diseases have altered in incidence and form and to the effect that modern methods of therapy have had on those diseases. It is not within my scope to discuss in detail the great advances made by recent research in our subject, as this would cover a vast field.

TABLE 1.—*Total Number of Patients Compared with Incidence of Warts*

	New Patients		Wart Cases		Eczema-Dermatitis Cases	
Yr.	No.	Exc. Warts, No.	No.	%	No.	%
1934	3,266	3,005	261	8	1,277	39
1935	4,194	3,889	305	7.2	1,340	32
1936	4,930	4,497	433	9	1,490	30.2
1937	5,050	4,614	456	9	1,883	37
1938	5,024	4,412	612	12	1,995	39.9
1939	5,050	4,462	588	11	No figures available	
1940	5,584	5,011	573	10.2	1,879	35.5
1941	5,625	5,024	591	10.5	1,874	33.1
1942	5,907	5,437	570	9.5	1,744	29.5
1943	5,606	5,091	515	9.2	1,882	33.6
1944	6,414	5,806	608	9.5	2,069	32.2
1945	6,143	5,548	595	9.7	2,175	35.4
1946	6,456	5,974	662	10.2	2,088	32.3
1947	5,885	5,120	765	13	1,626	27.6
1948	6,306	5,521	785	12.4	1,958	31
1949	6,705	5,526	1,179	17.6	1,947	28.1
1950	6,623	5,256	1,367	20.6	1,904	28.7
1951	6,911	5,373	1,538	22.2	1,814	26.2
1952	6,873	5,325	1,548	22.5	1,926	28
1953	7,562	5,745	1,827	24.1	2,215	29.3
1954	7,773	5,908	1,865	24	2,234	28.8
1955	7,773	5,474	2,299	29.6	1,991	25.6
1956	8,287	5,777	2,510	30.3	1,785	21.5
1957	7,921	5,259	2,662	33.7	1,654	20.9

The figures to which I shall refer are those of the Skin Department of the Royal Infirmary, Edinburgh, a hospital founded in 1730, in which many famous men, including Willan and Bateman, received their first medical training and which has been the parent hospital of notable medical schools in the New World. The southeastern portion of Scotland in which Edinburgh is situated has a population of 1,136,000, and the Royal Infirmary attracts patients from all over Scotland and from parts of

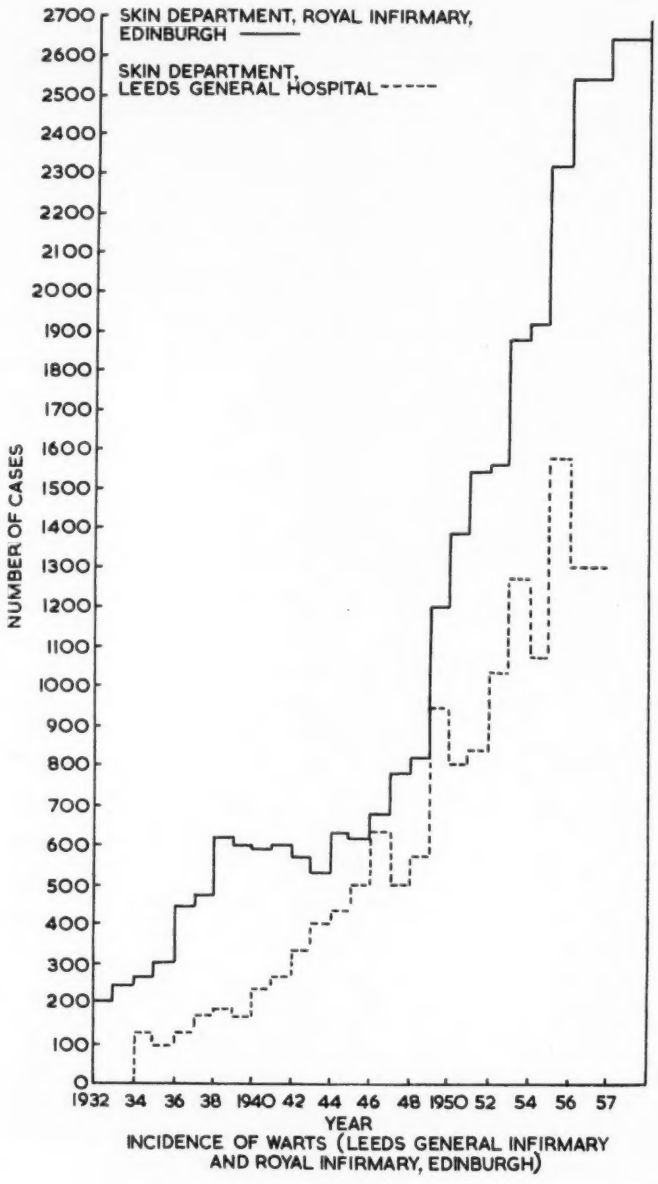


Fig. 1. — Incidence of warts.

England. The Skin Department, with five minor outpatient clinics at smaller peripheral hospitals, provides the dermatological service for this area.

Table 1 shows the total numbers of new outpatients seen at the Skin Department of the Royal Infirmary, Edinburgh, since 1932, and the number of cases of warts and eczema, which form such a high percentage of all patients. To us, *warts* are nothing but a squalid nuisance—we gain no kudos if we cure them, for anyone can cure a wart, but we are thought to be useless dermatologists if we fail, as not infrequently happens. Although we know so much about these excrescences, as yet we do not have any simple, effective cure, perhaps because rather than using destructive therapy we should pay more attention to the type of soil in which they flourish. Figure 1 shows how the incidence of warts has been increasing in two dermatological centers in Britain. I wonder whether there is any parallel to this in the United States or other countries. Vanished are the days when warts could be cured by almost any treatment, including suggestion; vanished too is the time when one could confidently treat them with x-rays in doses of 350 to 400 r. In 1931, just over 96% were cured with a single x-ray treatment, while 89.3% vanished with simpler methods, such as carbon dioxide snow, curettage, and formalin. Nowadays, such a high dosage is needed that one seldom employs radiotherapy at all. Instead, I find that the most effective treatment for verruca plantaris is 50% podophyllin resin in liquid petrolatum inserted deeply by means of a pointed orangestick, after which an occlusive dressing is applied for three weeks, when the wart can be readily removed. To this simple treatment may respond even the notoriously resistant mosaic warts, which were seldom seen in Britain before 1945, but which each year become commoner.

The *eczema-dermatitis* group, representing from 20% to 30% of all new patients examined, also accounts for a large number of those reporting on subsequent occasions, although so much has been done in the investigation of the various types. In allergic eczema, the work of Haxthausen,[1] Landsteiner and Chase,[2] Rostenberg,[3] Sulzberger,[4] and many others has helped to explain the mechanism of such reactions, and we look forward to the successes which will surely crown the research of the biochemists. However, the incidence of contact dermatitis is still rising because of the introduction of new chemical substances. One might well say: "Gone are the happy days of yore; when bottles of Eau d'Alibour and jars of Ung. Hyd. Ammon. dil. were cures for almost every ill. When every rash the skin revealed was Dermatitis if it healed; but if it went on uneffaced, 'twas ECZEMA —see Lassar's paste!"

There has also been an increase in the numbers of those cases in which many dermatologists ascribe mainly to psychosomatic factors, such as atopic and nummular eczema, but a decided reduction in seborrheic dermatitis and infectious eczematoid dermatitis, possibly due to the use of antibiotics. We must attribute the recent definite reduction in the total number of eczema cases to the introduction of hydrocortisone and related steroids, undoubtedly the most considerable advance in the symptomatic treatment of eczema for many years. But it is somewhat mortifying to realize that we still rely on the old standbys—silver nitrate, Burow's solution, compounds of zinc oxide and petrolatum, such as Lassar's paste, and, of course, crude tar. How many of us still use for eczema the elegant watermiscible creams or now confidently recommend even the most up-to-date barrier cream? Though we have abandoned them, antihistamine salves are still producing their quota of reactions, as are those containing local anesthetics, thanks to the power of advertising.

On the *pyodermias* the effect of modern therapy has been variable. Furunculosis and hidradenitis axillaris are by many still treated with antibiotics in serene confidence, despite relapses or the development of re-

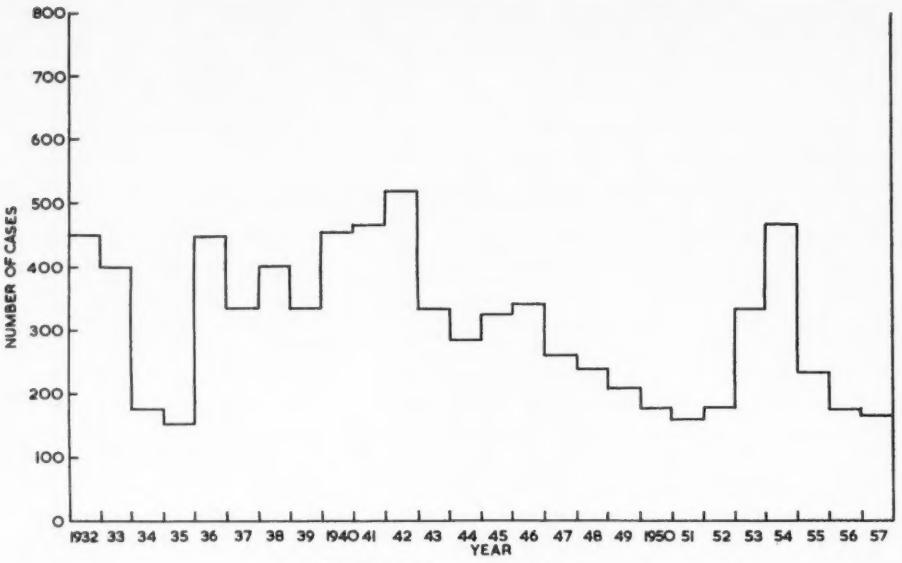


Fig. 2.—Incidence of impetigo.

sistant strains of Staphylococcus pyogenes var. aureus. I can recall in 1944-1945 treating with intramuscular penicillin a series of 200 soldiers suffering from chronic furunculosis. The immediate results were most impressive, but follow-up showed that practically all had relapsed, and many were worse than before. Sir Alexander Fleming realized that his penicillin had this drawback and knew that the ideal treatment for infections was one which not only cleared the infection but also increased the patient's resistance. Staphylococcal vaccine used properly is yet a most effective remedy. Unlike staphylococcal infections, streptococcal ones are vanishing. One seldom sees ecthyma these days, and the old impetigo contagiosa with its honey-colored crusts has practically disappeared. Prior to 1951, streptococcal impetigo was common in Edinburgh, but now it is seldom seen, its place having been taken by the once rare impetigo circinata. Figure 2 shows an epidemic of this reaching its peak in 1954. We have seen S. pyogenes var. aureus becoming resistant to penicillin and then to other antibiotics, such as chlortetracycline and oxytetracycline. We have observed the severe reactions to streptomycin, penicillin, and chloramphenicol; we have stopped using some antibiotics because of the danger of producing resistant organisms, and we now employ antibiotics not given by mouth or injection. Of these, in my experience, the French drug framycetin is by far the most effective, as one seldom, if ever, finds strains of staphylococci resistant to it; the enterobacteria, Pseudomonas pyocyanea, and the proteus group are highly sensitive to it, and I have yet to encounter sensitization to it. Because of the grave disadvantages associated with the use of antibiotics, we are reverting to the quinoline drugs we used in the thirties—quinolor, vioform, and chlorquinaloe (Sterosan)—often excellent but best prescribed in 1% strength or combined with hydrocortisone or prednisolone.

The incidence of *scabies* has fallen dramatically (Fig. 3) so that it is difficult to find examples to demonstrate to students. It will be observed that the number of cases increased from 153 in 1932 to 306 in 1938, reaching a peak of 859 in 1941 and steadily dropping to 31 in 1951. As Epstein[5] pointed out, this decrease has occurred in many countries, and, no doubt,

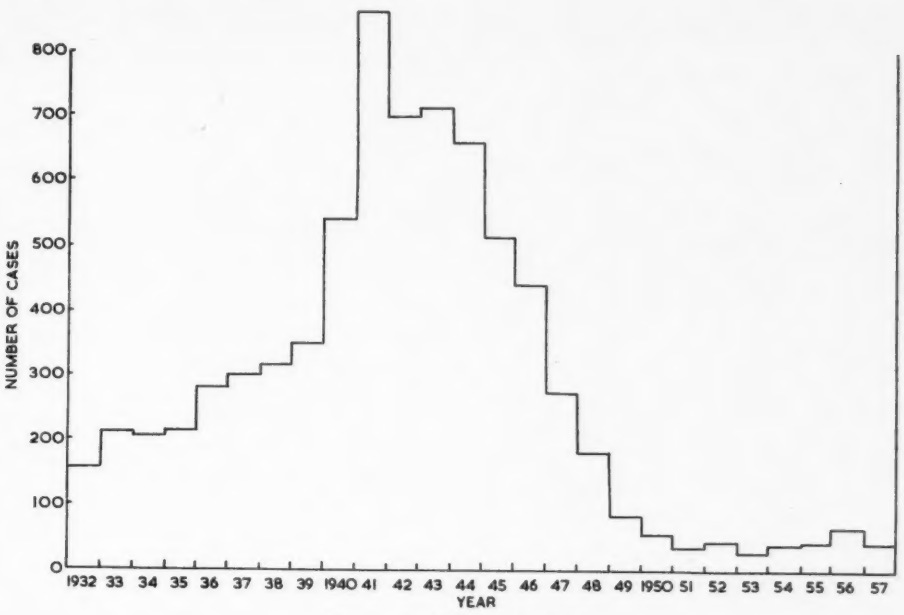


Fig. 3.—Incidence of scabies.

when a sufficient number of doctors are unable to diagnose the disease, the numbers will again rise. One cannot attribute the fall in incidence to improved methods of treatment; for example, benzyl benzoate has been used by me since 1933 after a visit

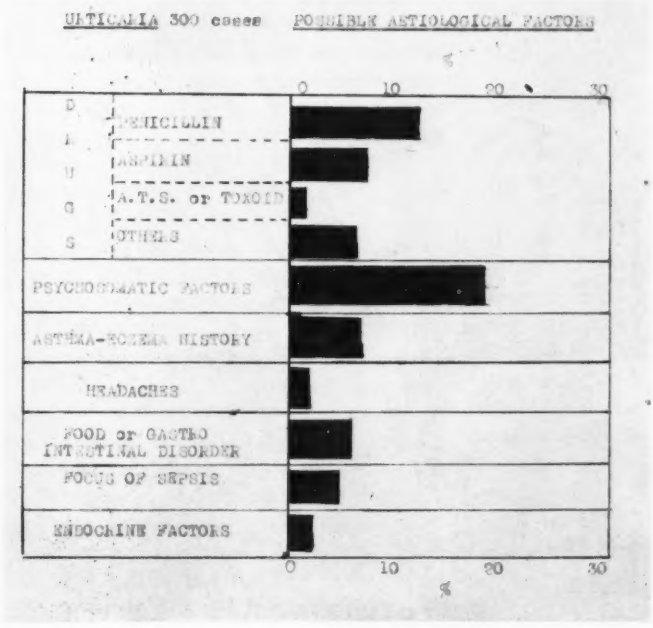


Fig. 4.—Causes of urticaria.

to Denmark, where it was introduced in 1906.

Urticaria is still unconquered and those of us who have suffered from it will sympathize with the description given by Samuel Pepys' diary in 1663—"whether the wind or cold did cause it or no I know not, but I have been this day or two mightily troubled with an itching all over my body which I took to be a louse or two that might bite me. I found this afternoon that all my body is inflamed and my face is a sad redness and swelling and pimpled."

In a series of 300 cases seen between the years 1953 and 1957, twenty-five per cent were caused by drugs, of which penicillin accounted for over half, many being extremely resistant to treatment (Fig. 4). In 68% of the 300 cases, urticaria had been present for over a month, and 1.5% had persisted for more than 10 years, imperfectly controlled by antihistamines. For such cases, the old-fashioned autohemotherapy had proved the most effective remedy. Too few physicians realize that antihistamines can only give symptomatic relief, have never yet cured a case, and in fact many cases of urticaria seem to persist even longer than they used to, in spite of, or perhaps because of, intensive and prolonged antihistamine therapy. The work of Grant, Comeau, and Pearson [6] on the production of wheals by the liberation of acetylcholine had led to many excellent studies on cholinergic urticaria and the influence of exertion, cold, and emotion in these cases, but no effective method of treatment has been established.

Even pediatricians are at least persuaded that urticaria papulosa in the great majority of cases is provoked by the bites of insects, thanks to the researches of dermatologists in Germany, U. S. A., and England and amply confirmed by the excellent therapeutic effect of D. D. T. or better still gamma-benzene hexachloride.

Twenty-five years ago syphilis and tuberculosis were the "great imitators," and, as Sir Robert Hutchison said, some doctors "looked at life through a syphilitic haze and would have given blue pills to the Vestal Virgins." Today, we seldom see cutaneous syphilis, and it is the possibility of a *drug eruption* that must be considered with every rash. A quarter of a century ago, the main drugs causing reactions were iodides, bromides, quinine, chloral, antipyrine, phenacetin, phenolphthalein, the heavy metals, salicylates, and barbiturates; today the number is legion, though as Alexander [7] pointed out, relatively few drugs are in common use, less than 1,000, and of them a small number account for the great proportion of rashes—barbiturates, sulfonamides, and antibiotics. Table 2 shows the causation of a series of cases seen as private visits, ones seen as outpatients, and ones seen in different departments of different hospitals.

TABLE 2.—*Cases of Drug Eruption Seen From Nov. 1, 1955, to April 31, 1956*

	No.	
Antibiotics		33
Penicillin	20	
Streptomycin	12	
Erythromycin	1	
Barbiturates & hydantoin compounds		12
Sulfonamides		13
Salicylates (including acetylsalicylic acid)		6
Phenolpthalein		5
Heavy metals		4
Gold	1	
Arsenic	1	
Mercury	2	
Halogens		3
Iodides	1	
Bromides	2	
Chloral		2
Chloroquin		1
Cocaine derivatives		1
Ephedrine		1
Liver injections		1
Nicotinic acid		1
Total no.		83

It is a sobering thought that all of us must have been responsible for causing misery to innocent patients by administering these "two-edged weapons." In 1947, Fisher,[8] from the Manchester area of England, wrote a paper on 65 cases of pink disease (erythedema), nine of whom died. He observed that no treatment was effective, but, since manufacturers have ceased using mercury in "teething powders," the disease has almost vanished. Many cases of Stevens-

Johnson disease are exacerbated by well-intentioned but ill-advised treatment with potent drugs. Seven cases of this condition treated by me all cleared within three weeks with no more potent therapy than oral nicotinic acid, as recommened by Weisberg and Rosen [9] for erythema multiforme. The remark of Voltaire that doctors pour "drugs about which they know little into bodies about which they know less" is indeed true and all too often we rely on entirely erroneous clinical impressions. Recently, some salutary papers have been published. For example, the heavy metals have for years been a standard form of therapy for lichen planus, yet Samman [10] showed that cases treated with oral arsenic and mercury did no better than the control series treated with a placebo and that there was a tendency to spontaneous cure within two years. Likewise, Epstein and Allington [11] demonstrated that in herpes zoster the effect of therapy is probably negligible, although we all no doubt have a simple faith in our favorite remedy.

In fact, for most *virus diseases* of the skin we have discovered no adequate therapy. Probably a study of cases of herpes simplex would show that all the treatments in vogue are of little avail. In the cure of molluscum contagiosum, the old methods—expression with forceps or cauterization with carbolic acid—are less painful and terrifying to the small child than fulguration. Although we know so much about the virus of this disease, there has been no reduction of the incidence of molluscum contagiosum. Who can explain why it should occur on the face in women and small children, although none in the household visit swimming baths? It is obvious why the growths are found on the trunk and upper limbs of boys.

During the past four years, there has been some decrease in the numbers of cases of *lupus erythematosus,* not only of the discoid but also disseminated types (Fig. 5), though no doubt more of the latter have been detected, thanks to the excellent researches in the United States on the L. E. cell. The prolongation of life in the disseminated cases has been paralleled by the successful results obtained in discoid cases with at first quinacrine and more recently chloroquine, amidoquine, and hydroxychloroquine sulfate (Plaquenil), the last-named being the most expensive, the least toxic, and often effective when the others have failed.

Another all-too-common dermatosis is *psoriasis,* the treatment of which has not advanced during the past quarter-century. Still the most effective are local remedies such as tar, ultraviolet light, and dioxyanthranol, and many psoriatics never seek the aid of a dermatologist, as they have been told the disease is incurable and that little can be done for them. New light on the etiology of the disease was shed by Gubner [12] in his paper on the treatment of psoriasis with aminopterin. His results have been confirmed by Rees B. Rees [13] and his coworkers. More recentiy, the work of Flesch and Esoda [14] has indicated that there appears to be abnormal cellular decomposition and abnormal utilization for keratin synthesis, due to deficient proteolytic enzyme activity in the epidermis. Since the early thirties of this century, the number of people who have developed psoriasis appears to be static, though there seems to be more atypical cases —more psoriasis-seborrhea of Unna, more

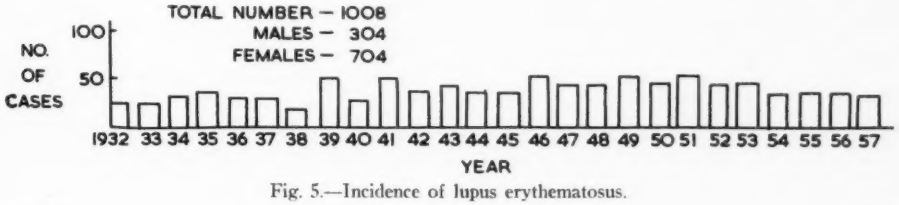


Fig. 5.—Incidence of lupus erythematosus.

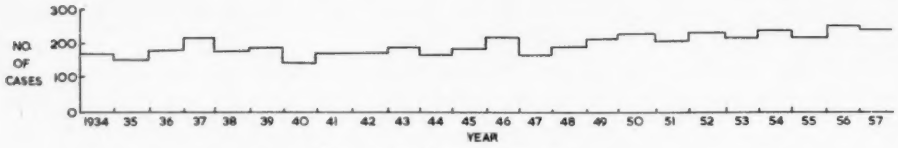


Fig. 6.—Incidence of psoriasis.

pustular psoriasis, more exfoliative cases, and more precipitated by drugs such as antibiotics (Fig. 6).

At long last doctors have realized that *acne vulgaris*, though it has a tendency to vanish when full adult life is attained, can not only leave disfiguring scarring but also has a profound effect on the patient's morale at the very age when he is most sensitive. This recognition may in part account for the apparent recent increase of this disease (Fig. 7). Few dermatologists have much faith in the effect of diet for acne, though recommending the exclusion of chocolate and the reduction of fats and carbohydrates. We still mainly rely on preparations containing sulfur and on x-rays in fractional doses and often obtain excellent results. Hormonal treatment has been decidedly disappointing, whether in the form of thyroid extract, estrin preparations, serum gonadotropin, and so on. Bullough [11] has demonstrated that in experimental animals, such as rabbits, certain steroids related to estrogens have no effect on sexual areas, such as vaginal epithelium, but have the same effect as estrogens in stimulating the rate of epidermal mitosis by their effect on the glucokinase system. I found that 73% of acne patients improved markedly after using for two months 1 mg. epioestriol per cubic centimeter of an inert lotion base compared with 45% of a control series using the base alone, but a larger series (now being studied) will be necessary to draw firm conclusions regarding the real value of this treatment.

Despite the introduction of new fungicides, *fungous infections* are far from being conquered. At the present time the incidence of tinea capitis is low after the postwar epidemic, but we cannot congratulate ourselves on this happy state of affairs, for, as in scabies, despite all our efforts, fresh epidemics are likely to occur, for we have

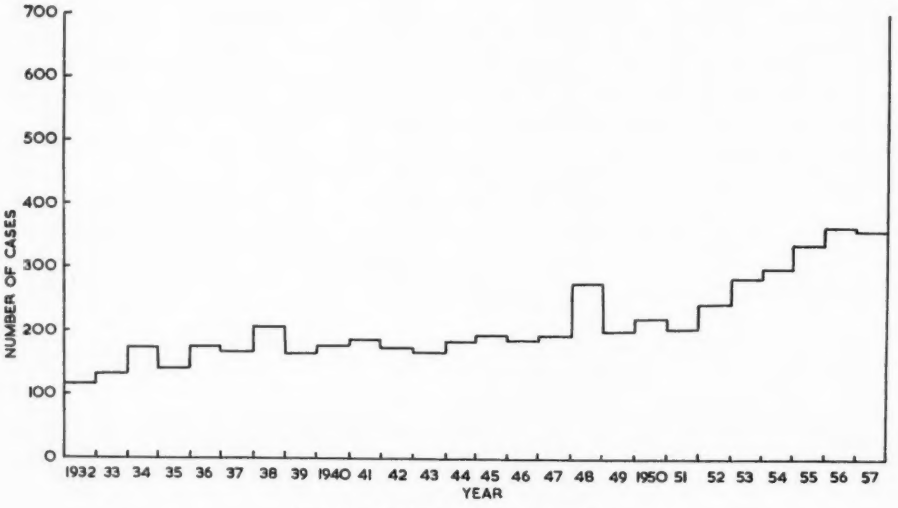


Fig. 7.—Incidence of acne vulgaris.

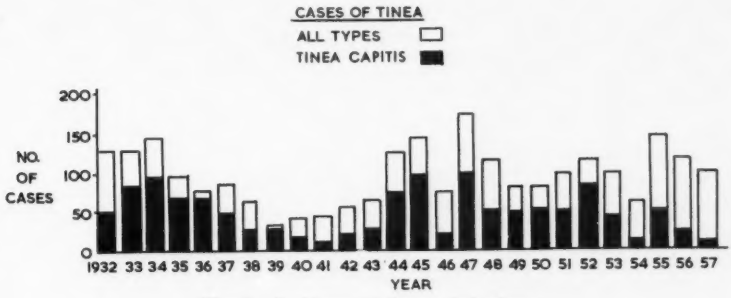


Fig. 8.—Incidence of fungus infections.

so few cases to demonstrate to our students (Fig. 8). In Scotland, animal ringworm is not uncommon and is usually due to Trichophyton mentagrophytes. Because of the pustulation associated with kerion formation, many doctors diagnose a secondary pyogenic infection and administer penicillin and other antibiotics. The exacerbation so produced has in some cases led to a degree of scarring never observed in prewar days. It is difficult sometimes to persuade the practitioner with little experience of this disease that sedative applications must be applied in the early phases. With the increased popularity of athletic pursuits, tinea pedis is becoming a problem even in Britain, with a climate disheartening to fungi. Higher fatty acid preparations, for which we owe gratitude to American pioneers like Rothman [16] and Peck,[17] have proved their efficiency with the additional advantage that they seldom cause contact dermatitis, but like you we have an increasing number of cases due to Trichophyton rubrum, affecting not only the feet but other areas.

Possibly the prevalence of infections due to Candida albicans is not altogether due to the universal use of antibiotics, as perionychia caused by yeasts was becoming more prevalent before the penicillin era, but undoubtedly oral antibiotic therapy is producing more and more cases of pruritus ani. In the treatment of these I have found the most effective remedy for local treatment to be ultracortenol with Bradosol cream, a combination of 0.05% domiphen bromide and 0.1% prednisolone. The domiphen bromide has a wide spectrum and in these cases is more effective than the quinoline drugs. The discovery of nystatin marked a real advance, as it is not only efficient against yeast infections but is remarkably free of side-effects. In vitro other antibiotics have shown strong fungicidal activity, but in mankind they have not proved their worth. In the United States, Blank [18] found that trichomycin, amphotericin B, and eulicin were the most promising. Some years ago I used trichomycin in a series of cases with no therapeutic effect whatsoever. Griseofulvin, in vitro and in experimental animals, is an effective fungicide, but in a controlled series of cases in a boys' boarding school Brewster and I [19] found that 1% griseofulvin ointment was no more effective than other fungicides. Yet it seems possible that in the future it may be feasible to cure ringworm by antibiotics administered by mouth or by injection.

The scourge of *tuberculosis* was, until recently, all too prevalent in Britain for many reasons—few cattle herds were tuberculin-tested; there was much malnutrition; in the big cities slums were very common, and there was little sunlight. During the year 1932, in our clinic 40 new cases of tuberculosis cutis were seen; in 1956, there were only six, three of them being lupoid reactions to BCG inoculations. We must realize that cases of cutaneous tuberculosis are seldom seen today, not because of the work of dermatologists, but because of general improvement in living conditions, the unremitting campaigns of the public health

authorities and, not least, the successful researches of big drug firms.

The *chronic bullous diseases* have aroused considerable interest in recent years, partly because they may be of serious import, partly because we at last have effective weapons to combat them, such as the corticosteroids. In my area of Scotland, true pemphigus vulgaris, confirmed by histology and the Tzank test, is somewhat of a rarity; what is called "benign pemphigoid" or even tautologically "bullous pemphigoid"—really senile dermatitis herpetiformis—is not uncommon, while juvenile dermatitis herpetiformis is far more often seen in the north of Britain than in the south. Though many elderly patients with benign pemphigoid require steroid therapy, it can be used in conjunction with other drugs, such as diaminodiphenylsulfone (Dapsone) or arsenic, and much smaller doses of each are required, and so side-effects are minimized. One recalls the days when the only effective treatment for Duhring's disease was arsenic and appreciates the difference drugs such as sulfapyridine, diaminodiphenylsulfone, and Promacetin (4,4′-diaminodiphenylsulfone-2-acetylsulfonamide) have made to the life of these sufferers.

The outlook for patients with Senear-Usher syndrome has been dramatically altered, for I have not yet seen a case which failed to respond to comparatively small doses of steroids.

Hemangiomata have been the cause of considerable discussion in dermatological circles in recent years, and I am one of those who hold stoutly to the view of Lister,[20] expressed in 1938, that cavernous angiomata should not be treated except on certain sites. It is difficult with some parents to withhold treatment from their child, but I have never yet regretted "masterly inactivity" in any of these cases, no matter how extensive they may be. One can however have sympathy with the mother who wishes an ugly blemish removed from her baby's face, and a light freezing with CO_2 snow is permissible, but not radium or x-rays. Even the radiologists have begun to realize this.

Capillary angiomata have not been treated by me personally by dermabrasion, as in Britain this procedure is mainly carried out by the plastic surgeons, but I can speak of the results of treatment with thorium X over a period of 12 years in a series of 54 cases. Although 21 mothers appeared to be convinced that the paint had had a beneficial effect, I was not fully convinced that there had been any real improvement, other than what might have occurred spontaneously, and in no case was there a really satisfactory cosmetic result, though two had almost recovered.

Carcinomata, basal cell, squamous cell, and intraepidermal, appear to have increased in number in recent years (Fig. 9), probably because of the increased expectation of life, and so many more live to develop them in old age. We have seen the replacement of the radium plaque by x-rays, but the high percentage of cures is not only due to efficient radiotherapy but also to the sound training of practitioners who recognize the

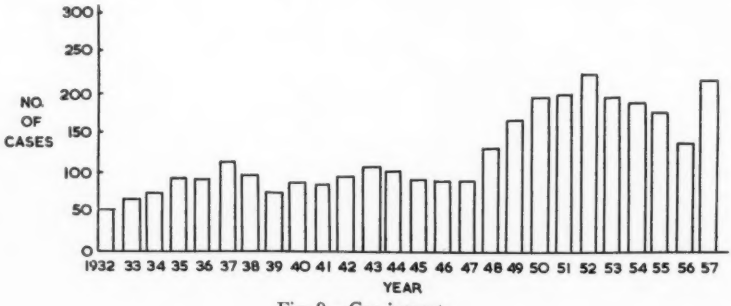


Fig. 9.—Carcinomata.

tumors at an early stage and insist on their patients' having treatment. There is no doubt that a proportion of basal-cell carcinomata heal spontaneously (and I do not include the superficial cicatrizing type), but the self-healing squamous-cell carcinoma of Ferguson Smith does not in the least resemble clinically the ordinary one, far less keratoacanthoma, which some writers appear to believe, very wrongly, is the same as Ferguson Smith's.

The subject of *keratoacanthoma* is a fascinating one. First described in 1930 by Dupont of Belgium [21] by the name *kyste sébacé atypique*, often referred to in Britain by the term "molluscum sebaceum" given to it by MacCormac and Scarff [22] in 1936, the title now generally used is that suggested by Freudenthal—keratoacanthoma. MacCormac and Scarff saw approximately 10 cases in 10 years, but since that time the tumor has become much commoner, and at the Edinburgh Royal Infirmary Skin Department there have been an average of 15 cases yearly for the past 6 years. Of these, I have seen five which recurred after they had been removed, and three of these became true invasive squamous-cell carcinomata and required radiotherapy. In any doubtful case it may be wise to take serial sections to exclude malignancy, for some portions of the tumor may show no invasive tendencies, while others undoubtedly do so.

Comment

In a review of the progress of dermatology over the past 25 years, what successes can be claimed and to what have they been due? It is sad to realize that we must confess to little progress toward the cure of the commonest dermatoses. Stress and heredity are such important factors in so many diseases that we must humbly acknowledge our comparative failure in coping as efficiently as we should with such conditions as atopic eczema, psoriasis, acne vulgaris, alopecia areata, and warts. These chronic and often unsightly disorders serve as a lasting reproach to us, and it is cold comfort to be told by laymen of cases of atopic eczema completely cured by an attack of enteric fever or a stubborn psoriasis which has vanished in a week following the fracture of an arm.

Credit must be given to drug firms for the cure of infective conditions such as tuberculosis, and many of our most effective modern remedies have been discovered by just those empirical methods, used, for example, by Withering when he employed digitalis infusion for heart disease. Examples which come to mind are the use of sulfapyridine and the sulfones in dermatitis herpetiformis and the newer antimalarials in lupus erythematosus.

How then does progress in dermatology compare with that in other fields of medicine? Much the same story comes to light. I quote the words of Nissen [23]:

> We are always being told by the newspapers (and in many scientific works as well) that doctors in the last fifty years have succeeded in the more highly developed countries, in raising the average expectation of life from 40 to 70 years. The figures are incontrovertible; what is false is simply the conclusion that this spectacular change is due to the achievements of medical science and to the efforts of the medical profession as a whole. The only branch of medical science that has made a substantial contribution to this statistical improvement is not gerontology but pediatrics; the truly progressive doctors are not those who look after the aged but those who keep our children alive. For it is essentially the tremendous decline in infant mortality that has raised the expectation of life to 70.

Dublin and Spiegelman [24] have demonstrated that the expectation of life of doctors over the age of 35 has increased by the bare fraction of a year, so that from the age 35 onward the prospective lifetime of a physician is somewhat less than for white people in the general population.

It is worth while considering how many of the remedies used 25 years ago have stood the acid test of time and how many have been superseded by newer methods. No longer are gold and bismuth used for lupus erythematosus; the Gerson diet and tuberculin, for lupus vulgaris; the toxic drug suramin (Germanin), for pemphigus—the

list could be multiplied again and again. But the old faithfuls such as Lassar's paste, Whitfield's ointment, and crude tar still hold their place. How many of our present-day treatments will be used in 1983? Will antibiotics and the steroids have vanished into limbo?

Yet our fathers obtained results not so inferior to our own, and some of the most able English dermatologists, such as Barber, Roxburgh, and Twiston Davies,[25] have been convinced that the modern shock-proof x-ray tube is not nearly so effective in the therapy of diseases such as eczema and warts as the old Coolidge one, and I am inclined to side with them. Perhaps it is not the apparatus but changes of the disease and of the soil on which it flourishes.

Though the present-day dermatologist is more conscious of the importance of psychosomatic medicine, he has as great faith in his favorite remedies as had his forefathers and possibly for as good reason. As Charpy [26] said, "The evolution of modern therapy is both wonderful and disquieting," but fortunately the effect of the placebo is as potent as it was in the 18th century. I have seen this happen in a series of patients with acne vulgaris in which the controls treated with a completely inactive lotion showed improvement in 45%. All dermatologists should read the paper on placebos written by Beecher,[27] who reviewed a selection of publications describing investigations using a placebo. Fifteen investigators treated 1,000 patients, and of these 35% responded favorably to the placebos for such things as headaches, angina pectoris, cough, sea-sickness, common cold, anxiety, and tension.

Faith can move mountains, and it is our duty to deserve the faith of our patients. It is important that we should not neglect the taking of a careful history from our patients. Though it may often be very illogical and inaccurate, it often sheds light on his character and environment and may act as a spiritual purgation for him. Bismarck is said to have objected to Schweninger asking him so many questions, to which the dermatologist's reply was, "Then you had better call in a veterinary surgeon." The doctor-patient relationship is just as important as it ever was, and most patients still prefer a physician who is dogmatic and confident, rather than one who gives in to his client's whims, such as his demand for the newest drug.

The most notable changes in incidences have been the fall in scabies and pyogenic infections, although more and more resistant strains of staphylococci have appeared; the virtual disappearance of tuberculosis of the skin; the control of diseases such as lupus erythematosus and dermatitis herpetiformis, and the prolongation of life in grave diseases such as exfoliative dermatitis, disseminated lupus, and the pemphigus group.

I have given the incidence of certain skin disorders seen since 1932 in a university clinic in Scotland, a very small facet of the dermatological universe. No doubt by themselves these figures are of little value, but, if a similar survey could be compiled in each country, some really valuable information regarding the etiology of some cutaneous diseases should be found. I, therefore, make the suggestion that a central registry of the incidence of diseases should be formed, similar, but on a larger scale, to that pioneered by Sagher for the pooling of information regarding urticaria pigmentosa.

As an example of the differences in certain countries, Dr. Onorio Carlesimo,[28] of the University Clinic of Rome, has informed me that in his city there has in recent years been a notable increase in dermatomyositis, poikilodermia of Jacobi, pemphigus vulgaris, and disseminated lupus erythematosus, whereas these have been few in number in Edinburgh during the past decade. On the other hand, in Italy they are fortunate in that atopic eczema is far less common than in our countries, and Dr. Carlesimo mentioned that Professor Crosti of Milan saw only a solitary case in 12 months. This reminds one of the low incidence of coronary sclerosis in Italy and its possible association with a diet low in animal fats.

Much more could be done in the prevention of skin diseases and there is often too

little cooperation with the public health authorities. By crusades similar to those against tuberculosis, the incidence of diseases such as scabies, pediculosis, tinea pedis, and warts could be greatly reduced. More postgraduate clinics especially for the family doctor could be established so that he could diagnose cases in the early stages and know when the aid of the dermatologist should be invoked. People today are too interested in themselves and their diseases, real or imaginary, so that they insist on having the newest drugs of which they have read or heard. We do too little to educate the public toward leading a life not likely to do harm to their skin, instead of inculcating into them the importance of such things as moderation in eating and drinking, the provision of adequate protection from all sorts of industrial hazards, the wearing of suitable clothing, and the necessity of "wearing life like a loose garment."

The past 25 years have seen great changes in dermatology, as in other branches in medicine, particularly in the understanding of disease processes, so that we have seen the overshadowing of histopathology by biochemistry and the discovery that the old idea of the bodily humors was in some ways true after all. That old sage Jonathan Hutchison [29] said, way back in 1884:

> Our forefathers, who knew far less about the details of pathology than we do, attached far more importance to such matters as temperament and diathesis. They were accustomed to prescribe for a man's temperament; we think only of his disease. . . . Although to a large extent this change of sentiment has been the result of advance of knowledge, yet I think it might easily be shown that it has gone too far, and that we now neglect unwisely the study of these differences between man and man of which, for the most part, physiology takes no cognizance, but which may yet prove of much importance in modifying the processes of disease.
>
> The idea of links between emotions and bodily states is very old. In the Hippocratic view, as much later in the James-Lange theory of the emotions, the production of a humour by an organ such as the liver created a corresponding emotional state. Lately the influence in the opposite direction has been emphasized, without specifying how the brain might irritate the skin into an eczema or the colon into ulceration. However, the discovery that the adrenal medulla under the influence of the sympathetic nervous system can liberate adrenaline and noradrenaline in varying ratios into the circulation, while the adrenal cortex under the influence of the hypothalmic-pituitary system can liberate hydrocortisone, offers a precise basis for influence in both directions. . . . Brain and adrenal interact, and both tissue and feeling may change.[30]

The future of dermatology lies in the hands of the histochemist, and those of us like myself, who have no training in, and far too little knowledge of, biochemistry, are thankful that the younger generation of dermatologists are in the vanguard in the unraveling of nature's problems.

Let us not, however, forget the words of a wise man named Robert Hutchison, who prayed:

> From inability to let well alone;
> From too much zeal for the new
> And contempt for what is old;
> From putting knowledge before wisdom,
> Science before art, cleverness before common-sense;
> From treatment of patients as cases;
> And from making the cure of the disease more grievous
> Than the endurance of the same;
> Good Lord deliver us.

The figures referred to in the text are taken from the records of the Skin Department, Royal Infirmary, Edinburgh, partly from my charge, and partly from that of Prof. G. H. Percival. Dr. P. W. Grant and Miss Sheena Stewart helped in correlating the figures. The illustrations were prepared by Mr. T. C. Dodds, F.R.P.S., Department of Medical Photography, Edinburgh University.

Skin Department, Royal Infirmary.

REFERENCES

1. Haxthausen, H.: The Eczemas, edited by L. J. A. Loewenthal, Edinburgh, Livingstone, Ltd., 1954, p. 112.

2. Landsteiner, K., and Chase, M. W.: J. Exper. Med. 69:767, 1939.

3. Rostenberg, A., and Kanof, N. M.: J. Invest. Dermat. 6:201, 1945.

4. Sulzberger, M. B.: Dermatologic Allergy, Springfield, Ill., Charles C Thomas, Publisher, 1940.

5. Epstein, E.: A. M. A. Arch. Dermat. 71:192, 1955.

6. Grant, R. T.; Pearson, R. S. B., and Comeau, W. J.: Clin. Sc. 2:253, 1936.

7. Alexander, H. L.: Reactions with Drug Therapy, Philadelphia, W. B. Saunders Company, 1955, p. iii.

8. Fisher, T. N.: Brit. M. J. 1:251, 1947.

9. Weisberg, A., and Rosen, E.: Arch. Dermat. & Syph. 53:99, 1946.

10. Samman, P. D.: Brit. J. Dermat. 68:175, 1956.

11. Epstein, E., and Allington, H. V.: A. M. A. Arch. Dermat. 76:408, 1957.

12. Gubner, R.: A. M. A. Arch. Dermat. & Syph. 64:688, 1951.

13. Rees, R. B.; Bennett, J. H., and Bostick, W. L.: A. M. A. Arch. Dermat. 72:133, 1955.

14. Flesch, P., and Esoda, E. C. J.: A. M. A. Arch. Dermat. 76:393, 1957.

15. Bullough, W. S.: Hormones and Mitotic Activity, in Vitamins and Hormones: Advances in Research and Applications, edited by R. S. Harris, G. F. Marrian, and K. V. Thimann, New York, Academic Press, Inc., 1955, Vol. 13, p. 261.

16. Rothman, S.; Smiljanic, A.; Shapiro, A. L., and Weitkamp, A. W.: J. Invest. Dermat. 8:81, 1947.

17. Peck, S. M., and Rosenfeld, H.: J. Invest. Dermat. 1:237, 1938.

18. Blank, H.: A. M. A. Arch. Dermat. 75:184, 1957.

19. Peterkin, G. A. G.: Practitioner 180:543, 1958.

20. Lister, W. A.: Lancet 1:1429, 1938.

21. Dupont, A.: Ann. Dermat. et syph. 81:621, 1954.

22. MacCormac, H., and Scarff, R. W.: Brit. J. Dermat. 48:624, 1936.

23. Nissen, R.: Geigy Bicentenary Day: Report of the Meeting, Basle, June, 3, 1958, p. 8.

24. Dublin, L. I., and Spiegelman, M.: J. A. M. A. 134:1211, 1947.

25. Davies, J. H. T.: Brit. J. Dermat. 68:22, 1956.

26. Charpy, J.: Dermatologic and Allergologic Therapy, Paris, Masson & Cie, 1957 (quoted from review by F. F. Hellier in Brit. J. Dermat.).

27. Beecher, H. K.: J. A. M. A. 159:1602, 1955.

28. Carlesimo, O.: Personal communication to the author, 1958.

29. Hutchison, J.: The Pedigree of Disease, London, J. & A. Churchill, 1884.

30. Editorial, Brit. M. J. 1:939, 1958.

Calcinosis Cutis: Its Relationship to Scleroderma

SIGFRID A. MULLER, M.D.; LOUIS A. BRUNSTING, M.D., and R. K. WINKELMANN, M.D., Rochester, Minn.

Calcinosis cutis denotes pathologic calcification in the skin. Although its association with scleroderma has been recognized for many years as the Thibierge-Weissenbach syndrome,[1] practically nothing is known about its incidence, time of onset, sites of predilection, or significance. Furthermore, the metabolic calcinosis in scleroderma has been confused with the metastatic calcinosis occurring in parathyroid disease. There are two general types of calcinosis: (1) metabolic calcinosis, associated with tissue injury, in which the concentrations of calcium and phosphorus in the serum are normal, and (2) metastatic calcinosis, in which the concentrations of calcium and phosphorus in the serum are elevated. The first type is the commoner type and occurs as a result of localized injury or as a manifestation of systemic disease, such as scleroderma or dermatomyositis. The second type rarely involves the skin, most commonly occurring in the lungs, stomach, and kidney. It is associated with hyperparathyroidism, intoxication with vitamin D, renal disease, and destructive bone lesions.

Elevated values of calcium in the blood, skin, and urine have been reported occasionally in patients with scleroderma, and parathyroidectomy has been done with supposedly significant amelioration of the disease.[2-10] The recent report of the beneficial effects of a new chelating agent, ethylene diamine tetraacetic acid (EDTA), in a patient with scleroderma[11] initiated our interest in the relationship of calcinosis to scleroderma. The intravenous administration of this new agent induces hypercalciuria and may temporarily lower the amount of calcium in the serum. Our experience with this drug in the treatment of patients with scleroderma is reported elsewhere.[12] The purpose of this project is to elaborate on the role of calcinosis in scleroderma and to reevaluate its relationship to parathyroid disease.

Method of Investigation

The records of 381 patients with scleroderma, seen at the Mayo Clinic from 1952 through 1956, were reviewed. For this study, the patients were grouped into the following three categories: (1) those having diffuse scleroderma, (2) those having acrosclerosis, and (3) those having morphea. Patients having diffuse scleroderma had central rather than peripheral sclerosis and involvement of other organs in addition to the skin; vasospastic symptoms, however, were not present. Patients having acrosclerosis had cutaneous sclerosis, which was more pronounced in the acral regions than elsewhere, and vasospastic symptoms in the extremities. The group was subdivided further into patients with severe or moderate acrosclerosis, according to the degree of Raynaud's changes, the extent of the sclerosis, and the evidence of visceral involvement. Those patients in whom acrosclerosis was of questionable severity were included with the group having severe acrosclerosis. A few patients in this last mentioned group had cardiac or pulmonary involvement. The group having morphea included those patients with a form of localized cutaneous sclerosis of a benign nature. It was subdivided into localized morphea, widespread morphea, and linear scleroderma. The conditions of these patients were reviewed, and the incidence, course, and location of calcinosis in each of the groups were tabulated. Evidence of parathyroid dysfunction was noted especially, as were the concentrations of calcium and phosphorus in the serum, the roentgenographic signs of para-

Submitted for publication Sept. 23, 1958.

Abridgment of thesis submitted by Dr. Muller to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Dermatology.

Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota. Fellow in Dermatology (Dr. Muller); Section of Dermatology (Drs. Brunsting and Winkelmann).

thyroid disease, and the history of renal calculi. Because of the interrelationships of serum calcium and serum magnesium (a decreased concentration of magnesium favoring calcification), determination of the value of serum magnesium was done when possible.[13]

Results

Incidence of Parathyroid Disease and Results of Laboratory Studies.—In no instance was evidence of parathyroid disease found clinically or roentgenographically. Only two patients gave histories of a single episode of renal lithiasis. Of the 23 patients having generalized scleroderma, 6 also had one or more determinations for serum calcium which gave normal results. Of the 230 patients with acrosclerosis, 51 had one or more determinations for serum calcium and phosphorus; results of all but 1 were normal.* The patient having abnormal results had acrosclerosis of severe degree and a value of calcium of 11.0 mg. per 100 cc. of serum. Two subsequent determinations, one and seven years later, gave normal results. This patient had small amounts of calcification in the fingers and shoulders. No explanation for the elevated value of serum calcium could be given, and parathyroid disease has not become evident subsequently. The concentration of serum calcium was slightly decreased in three patients, but these patients also had decreased values of serum albumin. Determinations of calcium and phosphorus in the serum proved to be normal for 10 of the 128 patients having various types of morphea for whom they were made.

Twenty patients had determinations for serum magnesium: fifteen in the group having acrosclerosis, one having generalized (diffuse) scleroderma, and four having morphea. The results of all determinations were considered normal and ranged from 1.66 to 2.25 mg. per 100 cc. Little is known about the range of normal concentrations of serum magnesium.[14]

Incidence of Calcinosis.—In 381 patients with scleroderma of all types, there were 277 females and 104 males, or a ratio of females to males of 2.7:1. Thirty-three patients had calcinosis, thirty females and three males, or a respective ratio of 10:1 (Table 1). One or more determinations for the values of serum calcium and phosphorus were done in 15 of these patients, and the results of all were normal.

There were 230 patients with acrosclerosis, 175 females and 55 males, or a ratio of about 3:1 (Table 1). Of the 230 patients, 98 had acrosclerosis of severe degree and 132 had acrosclerosis of moderate degree. Of the 230 patients, 31 had calcinosis, 28 females and 3 males, giving a ratio of 9:1 and an incidence of calcinosis in acrosclerosis of 13%.

In Diffuse Scleroderma: Calcinosis was not found in 23 patients with diffuse scleroderma. Of the 23 patients, 15 were women and 8 were men (Table 1). Scleroderma

* Normal levels of calcium and phosphorus at the Mayo Clinic range from 9.0 to 10.6 and 2.5 to 4.5 mg. per 100 cc. of serum, respectively.

TABLE 1.—*Distribution of 381 Patients with Scleroderma Seen at Mayo Clinic, 1952 Through 1956*

Diagnosis	Cases, %	Patients, No.					
		With Scleroderma			With Calcinosis		
		Total	Female	Male	Total	Female	Male
Diffuse scleroderma	6	23	15	8	0	0	0
Acrosclerosis	60	230	175	55	31	28	3
Moderate		132	100	32	5	5	0
Severe		98	75	23	26	23	3
Morphea	34	128	87	41	2	2	0
Localized		74	44	30	0	0	0
Widespread		18	15	3	1	1	0
Linear		36	28	8	1	1	0

had been present for an average of 1.8 years, with a median of 1 year and a range of 1 month to 10 years. The average age of the 15 women and 8 men was 48 years, with a median age of 47 and a range from 23 to 65 years.

In Acrosclerosis of Severe Degree: Of 98 patients with acrosclerosis of severe degree, the average age was 46.8 years, with a median of 47 years. On the average, when seen during the period 1952 to 1956, the disease had been present for 6.7 years, with a median of 4.0 years. Calcinosis occurred in 26 patients (27%) of this group. The average age at the time of diagnosis of calcinosis was 51 years, with a median of 53 years and a range of age from 10 to 69 years. The average duration of acrosclerosis before the diagnosis of calcinosis was 10.7 years, with a median of 10 years and a range of 1 to 23 years. Twenty-four patients had calcinosis in the hands; fourteen of these had calcinosis in the hands only, particularly in the fingers. Nineteen patients had calcinosis in the upper extremity only. Two had calcinosis involving the trunk. Four patients had soft-tissue calcifications in the lower extremities (Table 2). The largest deposits of calcium occurred in patients who gave histories of severe acrosclerosis present for more than seven years. However, there were several patients with long histories of severe involvement and only small amounts of calcium in the soft tissues. Only minimal deposits of calcinosis occurred when acrosclerosis was of short duration.

TABLE 2.—*Distribution of Calcinosis in Twenty-Six Patients with Acrosclerosis of Severe Degree*

Location	Cases, No.
Hands only	14
Hands	24
Upper extremity only	19
Lower arm to wrist	9
Shoulders	4
Lower portion of abdomen	1
Buttocks	1
Lower lumbar region	1
Lower extremities	4
Thighs	1
Knee to ankle	4
Chest	1

In Acrosclerosis of Moderate Degree: Calcinosis developed in 5 (4%) of 132 patients having acrosclerosis of moderate degree. Deposits were small to moderate in amount and were confined to the upper extremity. Two patients had calcinosis in the fingers only, and three, in the forearms and elbows only. The ages of these patients were 42, 54, 57, 58, and 64 years, and all were females. The duration of acrosclerosis in this group at the time of diagnosis of calcinosis was 1, 2, 5, 23, and 40 years. The largest quantities of pathologic calcification occurred in the two patients who gave histories of 23 years' and 40 years' duration of the disease.

In Morphea: There were no instances of calcinosis in the 74 patients with localized morphea, and only one instance, but that of severe degree, in the group of 18 patients with widespread morphea. This latter instance occurred in a 54-year-old white woman with a 20-year history of widespread morphea. She had taken 150,000 units of vitamin D daily from 1942 to 1945 and 50,000 units daily from 1945 to 1948. Extensive soft-tissue calcifications were discovered in 1948, in the hands, elbows, forearms, and hips.

Calcinosis developed in one of 36 patients with linear scleroderma. A 38-year-old woman had had linear scleroderma and hemiatrophy of the right lower extremity for 35 years. Myositis ossificans was diagnosed roentgenologically in the atrophied leg.

Comment

In our review of 381 patients with scleroderma of all types, we were not able to relate scleroderma to parathyroid disease, according to present-day concepts of parathyroid function. This finding is in agreement with findings of Beerman and Stokes,[15] Rothman and Walker,[5] and most American dermatologists. Also, we could not detect any abnormality in the metabolism of magnesium by measuring the amount of

magnesium in the serum in several of these patients; thus, we could not confirm the suggestion that abnormalities in magnesium metabolism may be present in scleroderma.[16]

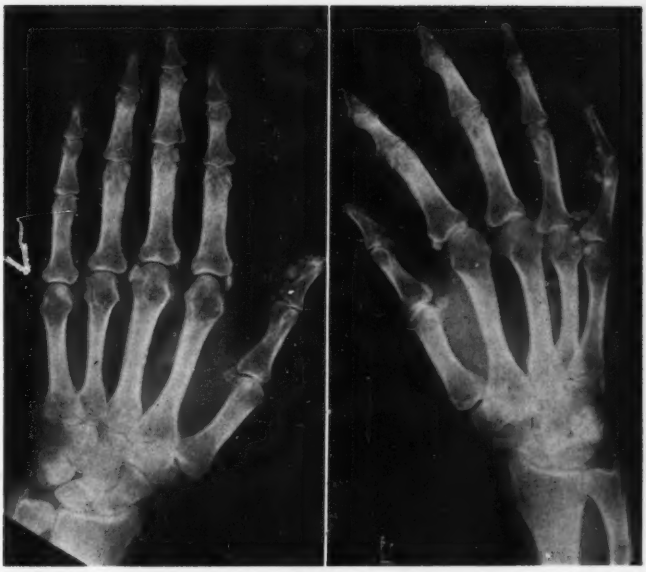
It has been shown recently that chondroitin sulfate, which is an integral part of the ground substance, may function as a cationic exchange resin and preferentially bind calcium ions without the occurrence of calcinosis.[17-20] Therefore, the earlier reports of increased amounts of tissue calcium in uncalcified sclerodermatous skin may have been accurate. This mechanism could circumvent the parathyroids and could explain at least part of the earlier confusion. Wheeler and associates[6] have suggested that the reports of negative and positive calcium balance in scleroderma were in complete accord. A positive balance meant only that calcium was being laid down at the sites of injury, while a negative balance indicated that resorption and healing predominated and that the excess urinary calcium was only temporary.

Of 381 patients with scleroderma of all types, there were 33 patients with calcinosis, for an over-all incidence of 8.7%. This incidence is in contradistinction to the rare incidence reported by Brody and Bellin[21] and Wheeler and associates[6] but in agreement with the incidence of 10% reported by Leinwand and his co-workers.[22] The females outnumbered the males 10 to 1, a sexual predisposition similar to that of calcinosis in dermatomyositis.[23] No differences in the severity of the disease were noted between females and males. The reasons for the increased incidence of calcinosis in females is unknown, but it should be remembered that estrogens do affect calcification in lower animals, as in the avian egg-laying cycle.[24]

In all but two instances calcinosis occurred in association with acrosclerosis. These latter two instances of calcinosis were associated with unusual circumstances: large, prolonged doses of vitamin D in one case and hemiatrophy of 35 years' duration in the other. It should be noted that Christianson[25] recently reported 5 cases of calcinosis in 64 patients with hemiatrophy secondary to linear scleroderma and no instances of calcinosis in 72 patients with the congenital and primary idiopathic forms of hemiatrophy. Christianson and associates[26] reported no instances of calcinosis in 83 patients with localized morphea and only one instance of calcinosis in 44 patients with widespread morphea. The latter instance is the same one we have reported. Thus, in our experience, calcinosis associated with scleroderma occurs only in acrosclerosis and linear scleroderma with hemiatrophy.

The incidence of calcinosis in 27% of the 98 patients with acrosclerosis of severe degree and in only 4% of the 132 patients with acrosclerosis of moderate degree shows that calcinosis developed almost seven times more frequently in patients with severe involvement than in patients with moderate involvement. The diagnosis of calcinosis was made on an average of 11 years after the onset of the disease. It seems probable that the incidence of calcinosis would have been much higher had we been able to follow all these patients at least 11 years. This long interval between onset of the disease and the diagnosis of calcinosis may have been due partly to the asymptomatic nature and small size of many of these calcified particles. However, the onset of calcinosis still was obviously greatly delayed in several patients in whom calcinosis developed, although they were under close scrutiny. There was no consistent correlation between the time of onset of calcinosis and the severity of the disease. Generally, the deposits of calcium were greatest in the patients with severest involvement; however, this was not always true.

It is difficult to decide on the exact prognostic significance of calcinosis in scleroderma because of the chronicity of the disease. Patients with calcinosis have usually already survived the acute manifestations of the disease for a long period and will naturally be a selected group with an improved outlook for survival. The occurrence of calcinosis in acrosclerosis appears to be the result of chronic injury to the



Evidence of soft-tissue calcification as a sequela of acrosclerosis.

soft tissues and may not necessarily indicate inactivity and healing. Furthermore, inactivity of the disease in the skin does not indicate inactivity of the disease elsewhere, since the disease occasionally has progressed in other parts of the body, including the viscera, in some patients with static or minimal involvement of the skin.

Pathologic soft-tissue calcification usually occurred in the acral portions of the upper extremity. Of 31 patients with calcinosis, 26 had involvement of the hands (Figure). Calcinosis was limited to the upper extremity in 75% and to the hands in 50%. Generally, the amount of soft tissue involved by calcification was not great. In only one patient could a diagnosis of calcinosis universalis be justified.

In our study, it became apparent that the term "calcinosis cutis" is often a misnomer. The exact site of calcification cannot be determined accurately by palpation and may be in the skeletal muscles. Furthermore, the abnormal deposits of calcium may be discharged periodically through the skin and may be found only temporarily in the cutis although their origin may have been elsewhere. Soft-tissue calcification also has been referred to as "interstitial calcinosis," [27] but this term does not offer any particular advantage.

The extrusion of calcium particles through the skin in patients with acrosclerosis is commonly observed to occur in the fingers, although it may occur much less commonly in other sites. Episodes of ulceration and extrusion of lime salts, although extremely painful, are not usually associated with severe systemic manifestations. This is in contrast to such episodes in patients having dermatomyositis; the patient frequently is severely incapacitated and confined to bed for several days or weeks till extrusion and healing have occurred. This contrast in reaction patterns is probably due to less extensive and more superficial deposits of calcium salts in acrosclerosis which effect less necrosis of tissue. It seems probable that the calcinosis in scleroderma has its origin primarily in the superficial tissues and not to any great extent in the skeletal muscles.

It is interesting to speculate on the absence of pathologic calcification in patients with diffuse scleroderma. In our experience, the absence of calcinosis characterizes pa-

tients with diffuse scleroderma. From our review, it is apparent that diffuse scleroderma is an uncommon form of scleroderma (less than 6% of our series). This difference is further magnified by the selection of patients seen at the Mayo Clinic. Patients with acrosclerosis occasionally follow a rapid downhill course and die; but more commonly, they give histories of long disability and are seen on several occasions, over several years. On the other hand, patients with diffuse scleroderma give histories of short disability, usually less than two years, and, due to the rapid progression of the disease, may not be seen again. In our experience, these two forms of systemic scleroderma are clinically distinct. The occurrence of calcinosis would also appear to justify separate recognition. Patients with diffuse scleroderma may not live long enough for calcinosis to develop.

Summary and Conclusions

The records of 381 patients with scleroderma of all types seen at the Mayo Clinic from 1952 through 1956 were reviewed, with particular attention to the relationship to parathyroid disease and the occurrence of calcinosis cutis. The following observations were made:

1. In the records reviewed, no clinical or laboratory evidence of parathyroid disease in scleroderma was discovered.

2. Calcinosis cutis occurred only in association with acrosclerosis, with rare exceptions.

3. Calcinosis cutis occurred much more frequently in patients with acrosclerosis of severe degree than in those with moderate involvement and occurred predominantly in females. It usually develops in the upper extremity, particularly in the hands. Calcinosis universalis is rarely a sequela of scleroderma.

4. Calcinosis is usually a late sequela in scleroderma. It is diagnosed on an average of 11 years after onset of the disease.

5. Patients having scleroderma with calcinosis probably have a more favorable outlook for survival than those who do not have calcinosis, because its appearance indicates chronicity of the disease.

Mayo Clinic.

REFERENCES

1. Thibierge, G., and Weissenbach, A. J.: Concrétions calcaires sous-cutanées et sclérodermie, Ann. dermat. et syph. 2:129-155, 1911.

2. Cornbleet, T., and Struck, H. C.: Calcium Metabolism in Scleroderma, Arch. Dermat. & Syph. 35:188-201 (Jan.) 1937.

3. Leriche, R., and Jung, A.: Recherche sur la nature de la sclérodermie: Les traductions tissulaires de l'hyperparathyroïdisme dans la sclérodermie: Ostéolyse: Surcharge calcique de la peau: Signification des chiffres indiquant la teneur en calcium du sérum et des urines, Presse méd. 43:1361-1363 (Aug.) 1935.

4. Leriche, R.; Jung, A., and Sureyya, C.: La peau dans l'hyperparathyroïdisme expérimental, Presse méd. 43:777-781 (May) 1935.

5. Rothman, S., and Walker, S.: Scleroderma, M. Clin. North America 33:55-77 (Jan.) 1949.

6. Wheeler, C. E.; Curtis, A. C.; Cawley, E. P.; Grekin, R. H., and Zheutlin, B.: Soft Tissue Calcification, with Special Reference to Its Occurrence in the "Collagen Diseases," Ann. Int. Med. 36:1050-1075 (April) 1952.

7. Bernheim, A. R., and Garlock, J. H.: Parathyroidectomy for Raynaud's Disease and Scleroderma, Ann. Surg. 101:1012-1025 (April) 1935.

8. Bernheim, A. R., and Garlock, J. H.: Parathyroidectomy for Raynaud's Disease and Scleroderma: Late Results, Arch. Surg. 38:543-555 (March) 1939.

9. Leriche, R.; Jung, A. and De Bakey, M.: The Surgical Treatment of Scleroderma, Surgery 1:6-22 (Jan.) 1937.

10. Ochsner, A., and De Bakey, M.: Scleroderma: Symposium: Surgical Considerations, New Orleans M. & S. J. 92:24-30 (July) 1939.

11. Klein, R., and Harris, S. B.: Treatment of Scleroderma, Sclerodactylia and Calcinosis by Chelation (EDTA), Am. J. Med. 19:798-807 (Nov.) 1955.

12. Muller, S. A.; Brunsting, L. A., and Winkelmann, R. K.: The Treatment of Scleroderma with the New Chelating Agent, EDTA, unpublished data.

13. Cantarow, A.: Magnesium Metabolism, in Duncan, G. G.: Diseases of Metabolism, Ed. 3, Philadelphia, W. B. Saunders Company, 1952, pp. 285-287.

14. Bodansky, M., and Bodansky, O.: Biochemistry of Disease, Ed. 2, New York, The Macmillan Company, 1952, pp. 1176-1177.

15. Beerman, H., and Stokes, J. H.: The Treatment of Scleroderma, Am. J. M. Sc. 217:453-461 (April) 1949.

16. Price, J. M.; Brown, R. R.; Rukavina, J. G.; Mendelson, C., and Johnson, S. A. M.: Scleroderma (Acrosclerosis): II. Tryptophan Metabolism Before and During Treatment by Chelation (EDTA), J. Invest. Dermat. 29:289-298 (Oct.) 1957.

17. Meyer, K., and Rapport, M. M.: The Mucopolysaccharides of the Ground Substance of Connective Tissue, Science 113:596-598 (May 25) 1951.

18. Neuman, W. F.; Boyd, E. S., and Feldman, I.: The Ion-Binding Properties of Cartilage, in Metabolic Interrelations with Special Reference to Calcium, edited by E. C. Reifenstein, Jr., and S. L. Wells, New York, Josiah Macy, Jr., Foundation, 1952, pp. 100-112.

19. Engel, M. B.; Joseph, N. R., and Catchpole, H. R.: Homeostasis of Connective Tissues, A. M. A. Arch. Path. 58:26-39 (July) 1954.

20. Engel, M. B.; Joseph, N. R., and Catchpole, H. R.: Equilibrium of Calcium and Other Ions in Connective Tissues, in Metabolic Interrelations with Special Reference to Calcium, edited by E. C. Reifenstein, Jr.; S. L. Wells, and B. B. Turner, New York, Josiah Macy, Jr., Foundation, 1954, pp. 105-118.

21. Brody, J., and Bellin, D. E.: Calcinosis with Scleroderma, Arch. Dermat. & Syph. 36:85-105 (July) 1937.

22. Leinwand, I.; Duryee, A. W., and Richter, M. N.: Scleroderma (Based on a Study of over 150 Cases), Ann. Int. Med. 41:1003-1041 (Nov.) 1954.

23. Muller, S. A.; Winkelmann, R. K., and Brunsting, L. A.: Dermatomyositis and Calcinosis, unpublished data.

24. Copp, D. H.: Calcium and Phosphorus Metabolism, Am. J. Med. 22:275-285 (Feb.) 1957.

25. Christianson, H. B.: Hemiatrophy Associated with Scleroderma and Other Conditions, Thesis, Graduate School, University of Minnesota, 1956.

26. Christianson, H. B.; Dorsey, C. S.; O'Leary, P. A., and Kierland, R. R.: Localized Scleroderma: A Clinical Study of 235 Cases, A. M. A. Arch. Dermat. 74:629-639 (Dec.) 1956.

27. Sunderman, F. W., Jr., and Sunderman, F. W.: Interstitial Calcinosis, Am. J. M. Sc. 234: 287-296 (Sept.) 1957.

Generalized Rhinosporidiosis with Visceral Involvement

Report of a Case

S. AGRAWAL, M.B.B.S., M.Sc. Path., Jabalpur, India; K. D. SHARMA, M.B.B.S., M.Sc. Path., Nagpur, India, and J. B. SHRIVASTAVA, M.D. (Bom.), D.B. (Lond.), Kasauli, India

Rhinosporidiosis, a chronic granulomatous infection due to Rhinosporidium seeberi, is reported to be endemic to India. It frequently involves the nasal passages, and infection at other sites, like ocular tissues, lip, urethra, larynx, rectum, and skin, although rare, has been reported. Generalized involvement of the skin is extremely uncommon. In such cases the spread of infection is thought to be due to autoinfection, caused by scratching the skin by fingers contaminated from the primary site. In a review of the available literature, we could come across only one case of generalized rhinosporidiosis due to hematogenous dissemination, producing visceral involvement.[8] We are reporting the second case of this nature because of its extreme rarity. Besides the generalized involvement of the skin, this case showed involvement of tongue, larynx, epiglottis, ocular tissues, liver, lungs, kidney, and spleen.

Report of Case

A Hindu man, aged 30 years, resident of District Raipur, Chattisgarh division, Madhya Pradesh, was admitted with the complaints of growth at the right lower lid for three years, nodules all over the body for one year, distention of the abdomen for four months, and edema of the feet for three months. On examination the patient was found to be a young man of fair build. Edema was present over the feet. There was no cyanosis or jaundice. The epitrochlear and inguinal glands were enlarged. There were multiple nodules over the chest, back, lower extremities, and scalp, varying from 0.5 to 2 cm. in diameter. Some of the nodules were ulcerated. There was no growth in the nasal passages, but a sessile growth about 3 cm. in diameter was seen on the palate. The abdomen was distended owing to free fluid in the peritoneal cavity. Liver and spleen were not palpable. A clinical diagnosis of mycosis fungoides was made. The investigations done were as follows: hemoglobin 60%, total red cell count 3,400,000 per cubic millimeter, total white cell count, 6,200 per cubic millimeter, differential leukocytic count showed polymorphonuclear cells 48%, lymphocytes 40%, monocytes 9%, and eosinophils 3%; erythrocytic sedimentation rate, 40 mm. in first hour (Wintrobe); Kahn test, negative; urine, normal; ascitic fluid, clear, straw-colored, with protein 2%; liver-function tests showed total protein 4.2 gm., albumin 2 gm., globulin 2.2 gm.; flocculation tests showed values within normal limits; serum bilirubin, 0.2 mg.; icterus index, 4 units; VDB reaction, indirect positive.

Biopsy specimens from the growth on the palate and on the right leg showed histological features of rhinosporidiosis. On March 15, 1957, the patient died suddenly, a few hours after liver biopsy was performed.

Autopsy Findings.—The relevant autopsy findings were as follows:

Pitting edema over feet was present. There was a small ulcerated nodule on the right lower lid. The nasal passages and nasopharynx were clear. A cauliflower-like sessile growth measuring about 3 cm. in diameter was present on the palate. Multiple small nodules, varying from 0.5 to 2 cm. in diameter were present on the chest, back, scalp, and lower extremities. Some of these were ulcerated.

Each pleural cavity contained 300 cc. of dirty brown fluid, and the peritoneal cavity, 1,200 cc. of similar fluid. The heart was normal. The right lung weighed 500 gm., and the left, 400 gm. Both

Submitted for publication Nov. 14, 1958.

Department of Pathology and Bacteriology, Medical College, Nagpur, India. Reader in Pathology, Medical College, Jabalpur, (Dr. Agrawal); Reader in Pathology, Medical College, Nagpur (Dr. Sharma), and Director, Central Research Institute, Kasauli (Dr. Shrivastava).

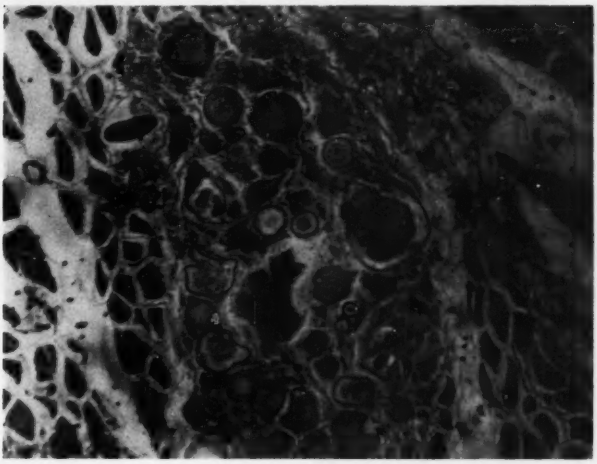


Fig. 1.—Photomicrograph showing infiltration of pectoral muscle by rhinosporidial granuloma (low power).

lungs showed small white nodules of firm consistency, which were seen on the external surface as well as on the cut surface. Liver weighed 1,175 gm. and was firm in consistency. The surface was pale and finely granular. The spleen weighed 525 gm. Cut surface showed Malpighian bodies to be prominent. Kidneys were normal. A nodule measuring 0.5 cm. was present on the posterior part of the tongue. A small papillary growth 3 mm. in size was seen on the free edge of the epiglottis, and growths of similar size were present on both vocal cords. The brain and spinal cord were not examined. The rest of the organs were normal.

Histology.—Nodules from the skin, eye, palate, tongue, epiglottis, and larynx showed similar features. The subepithelial lesions were crowded with large sporangia, measuring 200μ to 300μ in diameter. The sporangia had a thick double-lined chitinous wall. The fungus was seen in various stages of its life cycle, but mostly the spores were degenerated. Many of the sporangia were ruptured, liberating the spores into the tissues. The individual spores were 7μ-10μ in diameter and at higher magnification showed small granules. One of the nodules in the chest showed infiltration of the fungus into the underlying pectoral muscles (Fig. 1). The lungs showed formation of granulomatous nodules, situated in the interalveolar septae. There was a marked giant-cell reaction around the sporangia and the spores (Fig. 2). The spores and degenerated sporangia of R. seeberi were seen in the liver and the spleen (Figs. 3 and 4). The cellular response around them was negligible. In

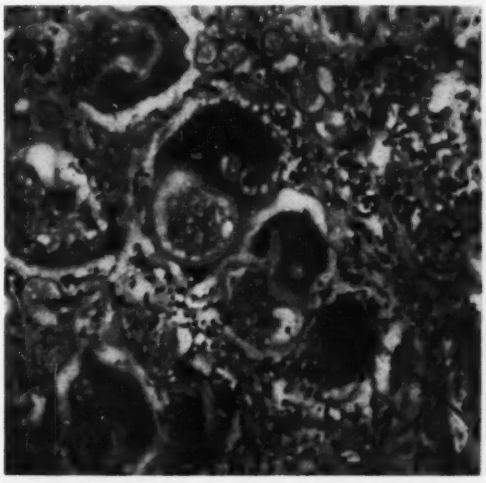


Fig. 2.—Photomicrograph showing rhinosporidial granuloma in lung. Note the foreign-body giant cells surrounding the sporangia (low power).

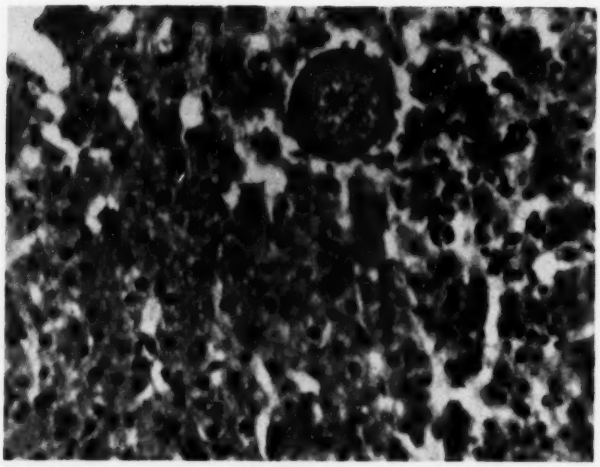


Fig. 3. — Photomicrograph showing a degenerating sporangium in liver sinusoid. Note the lack of cellular response (low power).

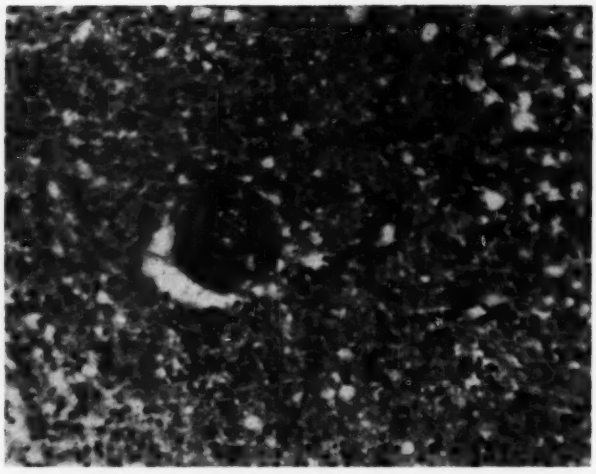


Fig. 4. — Photomicrograph showing a degenerating sporangium in spleen. Foreign-body giant cell more or less surrounds the sporangium (low power).

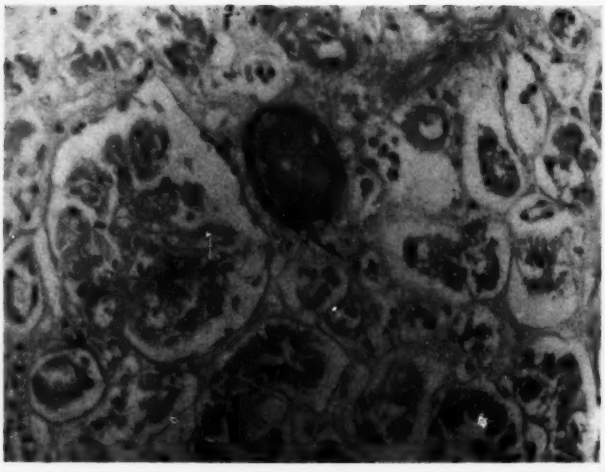


Fig. 5. — Photomicrograph showing degenerated sporangium in kidney. There is complete absence of cellular response (low power).

the spleen only in few fields an abortive attempt at giant-cell formation was seen. Besides, the liver showed early cirrhotic changes. The kidney showed few degenerated sporangia (Fig. 5).

Comment

The exact pathogenesis of rhinosporidiosis is as yet unknown. Many authors think that infection remains localized to the original site or in some cases may spread to neighboring areas by autoinoculation by the fingers and nails (Forsyth,[5] Karunaratne,[6] and Purandare and Deoras[7]). Allen and Dave[2] have reported cases with involvement of pharynx and larynx, and they believe that infection of esophagus and stomach can also occur by implantation. Dissemination of organisms through the lymphatic route would explain the lesions in areas away from the primary site, as in Dhayagude's[4] case.

A generalized hematogenous dissemination does not take place (Allen,[1] Karunaratne,[6] and Allen and Dave[2]). Castellani and Chalmers,[3] in 1919, admitted that R. seeberi could give rise to septicemia. Alessandrini (quoted by Simons[9]) saw for the first time a rhinosporidial infection in which a hematogenous route could be traced; the patient had a brain tumor, and a large number of spores of the fungus were found in the aspirated fluid from the tumor. Ruiz and Ocana (quoted by Simons[9]) observed spores of the fungus in the nasal blood vessels. The case reported by Rajam et al.[18] is interesting and unusual. In all it showed 33 cutaneous or subcutaneous lesions, the largest number occurring on the lower extremities. Spores of R. seeberi were demonstrated in the urinary sediment, laked peripheral blood, and ascitic fluid. The autopsy studies of the principal viscera failed to reveal any gross lesion. But microscopically the spores were demonstrated in kidney, liver, spleen, heart, pancreas, and brain. This is the first case where the diagnosis of hematogenous spread of the infection was established during life by the demonstration of parasite in the blood and body fluids and confirmed by the finding of the organism in many of the internal organs after death. The case reported by us showed rhinosporidial granulomata in the lungs and few scattered spores or degenerated sporangia in liver, spleen, and kidney as a result of hematogenous dissemination. Although the liver was cirrhotic, absence of gross and microscopic granulomata seems to rule out the possibility of rhinosporidial infection as the direct etiological factor in the causation of cirrhosis.

The visceral involvement with the formation of granulomatous lesions in the lungs is common in coccidioidomycosis. But the large, round, thick-walled, endospore-filled structures found in coccidioidomycosis are much smaller (80μ in diameter); the spores are smaller (2.5μ in diameter), and they do not contain the granules as seen in the spores of R. seeberi. Moreover, coccidioidomycosis is a disease of North America and South America. Proved cases of coccidioidal granuloma have been reported from Italy, the Balkans, Asia minor, and Hawaii; but these cases are very few. To the best of our knowledge, no proved case has been reported from India.

The diagnosis of rhinosporidiosis has been established in this case on the morphology of the fungus; large sporangia, measuring 200μ-300μ in diameter, filled with spores, nearly 7μ-10μ in size, showing uniformly sized granules, 1.5μ in diameter. Coccidioidin skin test was not performed during life; otherwise a negative skin test would have further confirmed the diagnosis of rhinosporidial infection.

Most of the papers on the subject of rhinosporidial infection deal with biopsy material, as the disease rarely endangers life. We believe that prolonged follow-up of all cases of proved rhinosporidial infection and opportunities for autopsy will reveal more cases of visceral involvement due to hematogenous dissemination.

Summary

A second case of generalized rhinosporidiosis with visceral involvement is recorded.

The available literature has been reviewed in brief.

Medical College, Nagpur (Bombay State), (Dr. Sharma).

REFERENCES

1. Allen, A. C.: The Skin: A Clinicopathologic Treatise, S. Louis, The C. V. Mosby Company, 1954, p. 494.

2. Allen, F. R., and Dave, M.: The Treatment of Rhinosporidiosis in Man: Based on the Study of 60 Cases, Indian M. Gaz. 71:376-393, 1936.

3. Castellani, A., and Chalmers, A. J.: Manual of Tropical Medicine, London, Bailliere, Tindall & Cox, 1919, pp. 533, 1578.

4. Dhayagude, R. G.: Unusual Rhinosporidial Infection in Man, Indian M. Gaz. 76:513-515, 1941.

5. Forsyth, W. L.: Rhinosporidium Kinealyi, Lancet 1:951, 1924.

6. Karunaratne, W. A. E.: The Pathology of Rhinosporidiosis Infection, J. Path. & Bact. 42: 193-202, 1936.

7. Purandare, N. M., and Deoras, S. M.: Rhinosporidiosis in Bombay, Indian J. M. Sc. 7: 603-610, 1953.

8. Rajam, R. V.; Viswanathan, G. S.; Rao, A. R.; Rangiah, P. N., and Anguli, V. C.: Rhinosporidiosis: A Study with Report of a Fatal Case of Systemic Dissemination, Indian J. Surg. 17:269-298, 1955.

9. Simons, R. D. G. Ph.: Handbook of Tropical Dermatology and Medical Mycology, Amsterdam, Elsevier Press, Inc., 1954, p. 378.

Psoriatic Arthritis

A Comparative Study of Rheumatoid Arthritis, Psoriasis, and Arthritis Associated with Psoriasis

V. WRIGHT, M.D., M.R.C.P., Baltimore

Since Alibert [1] first drew attention to the association of psoriasis and arthritis, in 1822, there have been numerous papers on the subject, usually describing single cases. Many attempts have been made to define the entity which has been variously called arthropathic psoriasis, psoriatic arthropathy, arthropathia psoriatica, and psoriatic arthritis. Some definitions have required a reasonable amount of synchronous activity, as evidenced by remissions and relapses in arthritis and cutaneous manifestations,[2] arthritis restricted to the distal interphalangeal joints,[3] or, conversely, a peculiar destructive form of arthritis associated with psoriasis.[4] Hensch[5] defined it as an atrophic arthritis following long continued and uncontrolled psoriasis, while Dawson [6] felt that the cutaneous lesions and joint changes must both be atypical.

Most published reports have dealt with cases fulfilling one or other of these diagnostic criteria, and broad surveys of the general field of concomitant psoriasis and joint disease have been few. Thus, Sherman,[7] in her excellent review, excluded many cases because she considered them to be coincidental rheumatoid arthritis and psoriasis but did not state her criteria of differentiation. Similarly, single cases have usually been reported because they fitted into one of the patterns outlined in the above definitions or else because they showed some striking feature, such as gross bone destruction. Such cases have colored later reviews, as often they have been added to the author's material to produce a larger survey but one which was highly selected.

It is difficult to estimate the incidence of the association of the two diseases. Depending on which feature predominates, the patient may fall into the hands of the dermatologist or the rheumatologist and escape the statistical eye of the other. It is not surprising that much argument has ensued on this score. Many believe the relation to be significant,[3,8] while other disagree.[9] The figures of those claiming an association often only border on statistical significance and are of little value in deciding a causal connection.

In recent years workers with the Rose-Waaler sheep cell agglutination test (S. C. A. T.), which is positive in 80% of patients with rheumatoid arthritis,[10] have observed that most patients who had psoriasis and atrophic arthritis had a negative test.[10,11] From a previous study of 39 patients with psoriasis and erosive arthritis it was suggested that those patients who had a negative S. C. A. T. either had rheumatoid arthritis modified by the presence of psoriasis or, more likely, were a distinct entity.[12] The series, however, only allowed tentative suggestions and did not permit statistical analysis; nor were control groups studied. A larger series has, therefore, been analyzed and compared with control groups of patients with uncomplicated rheumatoid arthritis and uncomplicated psoriasis, respectively, in an attempt to resolve some of the present conflicting views.

Material and Methods

One hundred fifty-four patients with psoriasis and various rheumatic complaints have been studied.

Submitted for publication Oct. 31, 1958.

University Department of Clinical Medicine, Leeds, England.

Ninety-five of the patients with psoriasis and erosive arthritis were paired with patients of the same sex and age who had uncomplicated rheumatoid arthritis of the same duration and a positive S. C. A. T. Eighty-five of the patients with psoriasis and erosive arthritis were paired with patients of the same age and sex who had uncomplicated psoriasis of the same duration. The modification of the S. C. A. T. introduced by Greenbury, Hill, Spalding Smith, and Good[10] was done with the serum of all patients. The purpose of this paper is to deal mainly with the dermatological manifestations and summarize the arthritic features.

General Review of Results

There were 23 patients with osteoarthritis, 2 with gout, 2 with rheumatic fever, and 9 with muscular rheumatism. They showed no unusual features of the skin or joint condition, and their association seemed fortuitous.

Of 118 patients with psoriasis and erosive arthritis, 41 were men and 77 women. Both rheumatoid arthritis and psoriasis are commoner in women, and these figures do not differ significantly from the sex incidence in other series of patients with psoriasis [8] and rheumatoid arthritis.[13] Clinically, the patients fell into three groups. Twenty-two (ten men, twelve women) had distal interphalangeal joint involvement primarily and nail changes of the same digit ("distal joint arthritis"). They had a negative S. C. A. T. A second group, of 10 paients (4 men, 6 women), had severe deformity due to ankylosis and disorganization of many joints, which had progressed to arthritis mutilans in four ("deforming arthritis"). All had a negative S. C. A. T. A third group, of 86 patients, had an arthritis clinically indistinguishable from rheumatoid arthritis. Yet 66 (77%), of whom 18 were men and 48 women, had a negative S. C. A. T., and they were considered as a separate entity ("indistinguishable arthritis"). In 20 (9 men, 11 women), the S. C. A. T. was positive, and it was thought they were examples of coincidental rheumatoid arthritis. The S. C. A. T. was negative in all patients with uncomplicate psoriasis.

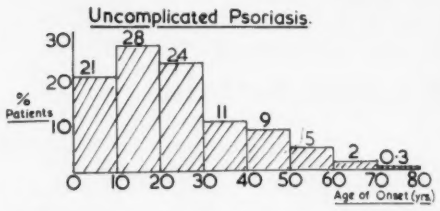


Fig. 1.—Age of onset of psoriasis in 310 unselected patients with uncomplicated psoriasis.

Onset of Psoriasis

There was no significant difference in the age of onset of psoriasis in any arthritic group when analyzed by decades and compared with 310 unselected patients with uncomplicated psoriasis (Fig. 1) and Ingram's series of 1,346 patients with psoriasis, which contained some having arthritis.[8] The average age of onset of psoriasis in patients with indistinguishable arthritis was 29.9 years. This did not differ significantly from any other group (Table 1).

The onset of skin lesions was acute in 20% of patients with uncomplicated psoriasis. It was accompanied by constitutional disturbance in 12% and pyrexia in 3%. None of these features differed significantly from those with arthritis. In 9% of patients with uncomplicated psoriasis the onset of the skin rash was preceded by tonsillitis, an incidence similar to that of the arthritic groups. Skin lesions began on the elbows, knees, or other parts of the legs most commonly (Fig. 2). In those with distal joint arthritis the nails were involved initially more frequently than in psoriasis ($P<0.01$), but the legs were less commonly affected at the onset ($P<0.05$).

Arthritis

The onset and course of arthritis in the 20 patients with psoriasis and erosive arthri-

TABLE 1.—*Average Age at Onset of Psoriasis in Patients with Erosive Arthritis* *

Arthritis	Male	Female	Total
Distal joint	23.5±4.1	34.8±5.7	29.4±3.7
Deforming	28.8±5.8	31.3±9.6	30.2±5.9
Coincidental rheumatoid	32.9±5.5	27.2±6.3	29.7±4.3
Indistinguishable	25.4±4.7	25.8±2.2	29.9±1.8

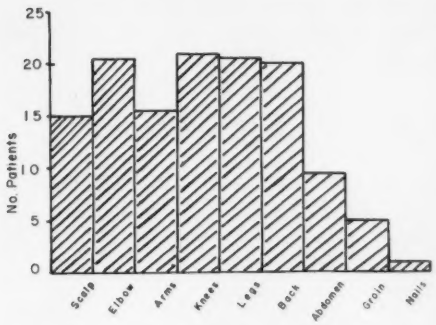


Fig. 2.—Site of onset of psoriasis.

tis who had a positive S. C. A. T. was the same as in those with uncomplicated rheumatoid arthritis. Subcutaneous nodules were present in 20%, an incidence similar to that of uncomplicated rheumatoid arthritis in both this and other authors' series.[3,11] Since these are regarded as the most characteristic lesion of rheumatoid arthritis,[3] and they were absent in the other groups, it supports the suggestion that these patients have coincidental psoriasis and rheumatoid arthritis.

The onset of arthritis in the distal joint group was more often insidious (77%), and, unlike the other groups, it commonly began in the terminal interphalangeal joints (59%). The arthritis was more often asymmetrical (36%) than in any other group and in half the patients resembled gout at some stage. It was, however, less painful than rheumatoid arthritis and less disabling. In only one patient was the arthritis limited to the distal joints, and there seems no justification for restricting the term psoriatic arthritis to those in whom it is.

The deformed group was characterized by an earlier average age of onset (26.6± 3.4 years) than coincidental rheumatoid arthritis (42.6±2.4 years; $P<0.01$), the arthritis beginning in most before 30 years of age. The onset in men was often accompanied by constitutional disturbances (75%) and pyrexia (50%). The worst deformity in any type of arthritis occurred in this group. The hips were involved significantly more often than in the other groups; the sacroiliac joints were involved radiographically in six, and the neck was the second commonest site listed as the worst place to be affected. Despite this the patients experienced significantly less pain than in rheumatoid arthritis.

The indistinguishable group had an average age of onset (33.9±1.8 years) significantly earlier than coincidental rheumatoid arthritis (42.6±2.4 years; $P<0.02$). The distribution of affected joints was the same as that in rheumatoid arthritis (i. e., the metacarpophalangeal, proximal interphalangeal, and metatarsophalangeal joints were most often involved), but most joints were less frequently involved. There were less muscular wasting, fewer examples of ulnar deviation, and less disability during the course of the arthritis, and functionally the patients were better than those with rheumatoid arthritis.

Family History

A family history was considered positive if the disease occurred in parents or siblings. Thirty-three per cent of patients with uncomplicated psoriasis had a family history of psoriasis. There was no significant difference in patients with psoriasis and arthritis, but all these groups differed markedly ($P<0.01$) from uncomplicated rheumatoid arthritis, in which a family history occurred in 2% (Table 2). A family history of rheumatoid arthritis was commoner in patients with uncomplicated rheumatoid arthritis than those with uncomplicated psoriasis ($P<0.01$). There was no significant difference in the frequency of such a family history between those with uncomplicated rheumatoid arthritis and the groups with psoriasis and arthritis. The significance of this is difficult to evaluate because of the small figures in some groups, the fact that the diagnosis of the arthritis in relatives depended on the patient's story, and the inability to correlate it with results of the S. C. A. T. in relatives. It is of interest that a family history of psoriatic arthritis was commonest in the deformed group. A

TABLE 2.—*Percentage Family History of Rheumatic Complaints and Psoriasis in All Groups*

Group	Family History, %						Patients, No.
	Psoriasis	Rheumatoid Arthritis	Osteoarthritis	Rheumatic Fever	Muscular Rheumatism	Psoriatic Arthritis	
Distal joint	50	14	18	17	45	4	22
Deformed	40	—	20	10	10	30	10
Coincidental rheumatoid	35	10	20	10	50	5	20
Indistinguishable	24	12	17	23	27	6	66
Uncomplicated rheumatoid	2	24	17	8	29	—	95
Uncomplicated psoriasis	33	6	11	15	20	2	85

family history of psoriatic arthritis was significantly commoner in patients with psoriasis and erosive arthritis having a negative S. C. A. T. than in uncomplicated rheumatoid arthritis or uncomplicated psoriasis ($P<0.01$). There was no signicant difference in this respect between the groups with psoriatic arthritis. The only other difference in the family history was that rheumatic fever was commoner in the indistinguishable than in the rheumatoid group ($P<0.01$).

Nail Changes

In patients with psoriasis (including some with arthritis) the nails are said to be involved in 10% to 25%, the figure of 15% being about the average in the literature. In the present group with uncomplicated psoriasis nail changes occurred in 32% (Table 3). Changes were present more frequently when erosive arthritis occurred with psoriasis, 81% ($P<0.01$). Since nail changes were almost as common in coincidental rheumatoid arthritis, it may be that such changes are nonspecific, occurring with any type of erosive arthritis. There seemed a more distinct relation in the distal joint group, however. Nail changes were invariably present in these patients, and in two the nails only were involved. In eight there was a marked topographical association between nail and distal joint changes (Fig. 3).

The changes involved the fingers and toes about equally, and in those with arthritis they were confined to the fingers in 11% and to the toes in 13%. In patients with uncomplicated psoriasis having nail changes hyperkeratosis was the commonest change (89%), then pitting (81%) and ridging (59%). It was difficult to assess the incidence of discoloration per se, and figures for this have not been included in the summary of the findings (Table 3). In the indistinguishable group hyperkeratosis was signicantly commoner than pitting ($P<0.02$) and ridging ($P<0.01$). This was also found in the distal joint group ($P<0.01$). When the types of nail change between the groups were compared, pitting was significantly commoner with uncomplicated psoriasis than with indistinguishable arthritis ($P<0.05$) and with distal joint arthritis ($P<0.01$). Ridging was significantly commoner with uncomplicated psori-

TABLE 3.—*Percentage Types of Nail Changes in Various Forms of Arthritis Compared with Uncomplicated Psoriasis*

Type of Arthritis	Nail Changes, %				Patients, No.
	Present	Pitting	Hyperkeratosis	Ridging	
Distal joint	100	41	100	41	22
Deforming	90	50	80	30	10
Coincidental rheumatoid	70	40	60	35	20
Indistinguishable	79	45	64	21	66
Uncomplicated psoriasis	32	22	24	22	85

Fig. 3.—*A*, topographical association of psoriatic nail changes and distal joint arthritis. *B*, contrast of affected and unaffected nails with topographically related distal joint arthritis in a patient with psoriasis.

asis than with indistinguishable arthritis ($P<0.01$). Hyperkeratosis was significantly commoner in the distal joint group than with indistinguishable arthritis ($P<0.02$).

There was no significant difference in the average age of onset of nail changes between the groups.

In some ways joint changes were more closely related to lesions of the nails than of the skin. There was a simultaneous onset of arthritis and nail changes oftener than of arthritis and skin lesions (Fig. 4; $P<0.01$). This closer relation was particularly marked in the distal joint group. In these patients nail changes often ushered in the psoriasis (27%), a much commoner mode of onset than in uncomplicated psoriasis (2%; $P<0.01$). A synchronous onset of nail and distal interphalangeal joint changes occurred in the majority but never with skin changes (Fig. 5). A synchronous exacerbation of nail and joint condition (73%) was twice as common as a synchronous exacerbation of skin and joint condition (36%), a highly significant difference ($P<0.01$). An inverse relation between skin and joint lesions was seen as commonly as a synchronous exacerbation in all groups.

Skin Lesions

In the literature the skin lesions have been described as extensive,[14] frequently involving the palms or soles and often pustular.[15] In this series the distribution of skin lesions on examination is shown in Table 4. The skin rash was symmetrical in about 90% of

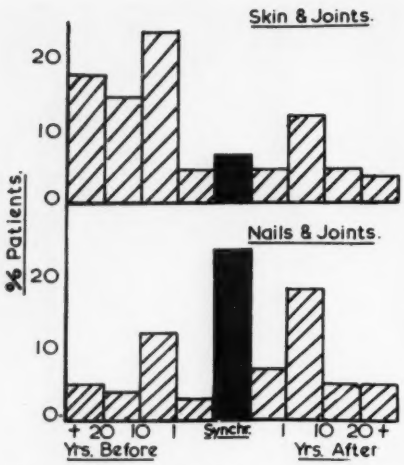


Fig. 4.—Onset of arthritis related to onset of skin and nail changes in patients with psoriasis and erosive arthritis.

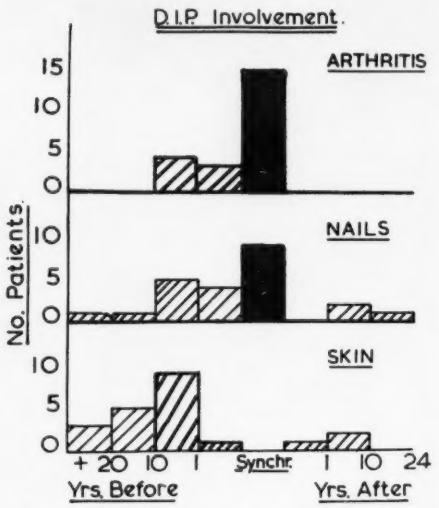


Fig. 5.—Onset of distal interphalangeal joint involvement related to the onset of arthritis, nail, and joint changes.

patients of all groups. The rash was most extensive in patients with deforming arthritis. The trunk was significantly less frequently involved in the distal joint group ($P<0.02$) and in the indistinguishable group ($P<0.01$) than in the uncomplicated psoriatic group. There was no significant difference in involvement of palms or soles in any group. The fingers had skin lesions more frequently in the deformed and indistinguishable groups than did patients with uncomplicated psoriasis ($P<0.01$). Lesions on the toes were commoner in the deformed and distal joint groups than in the uncomplicated psoriatic group ($P<0.01$). The degree of disability suffered by patients from psoriasis throughout the course of the disease was graded as mild, moderate, and severe; 30% of patients with deforming arthritis suffered severe disability, significantly more than the indistinguishable group (3%; $P<0.01$) and distal joint group, none of whom were severely involved ($P<0.02$). It can be seen that severe arthritis tended to be accompanied by extensive psoriasis.

The elbows and legs were more severely involved in patients with uncomplicated psoriasis than in those with distal joint arthritis. Conversely, the nails gave more trouble with distal joint arthritis than with uncomplicated psoriasis and indistinguishable arthritis. With deforming arthritis the legs were more frequently the site worst involved than with uncomplicated psoriasis, indistinguishable arthritis, and distal joint arthritis.

Guttate lesions were commoner with uncomplicated psoriasis (24%) than with in-

TABLE 4.—*Distribution of Skin Lesions in Patients with Psoriasis*

Group	Sites Involved, % Patients							Patients, No.
	Scalp	Trunk	Limbs	Palms	Fingers	Soles	Toes	
Distal joint	77	59	73	—	14	6	23	22
Deforming	80	100	100	10	40	10	30	10
Coincidental rheumatoid	55	65	85	10	25	—	15	20
Indistinguishable	64	65	82	12	12	3	3	66
Uncomplicated psoriasis	74	83	95	6	6	2	3	85

distinguishable arthritis (13%; $P<0.02$), but there were no significant differences between any other groups. Pustular psoriasis was significantly commoner with deforming arthritis (20%) than uncomplicated psoriasis (2%; $P<0.01$).

Treatment

Although the evidence suggests that there is a close relation between psoriasis and arthritis in some patients, the joint and skin lesions required independent treatment. There was little to confirm the suggestion that the arthritis will subside with adequate treatment of the skin.[2] In only 10 of the 118 patients was such a regression experienced.

Contrary to some reports,[16] the psoriasis was not usually resistant to treatment. There was no significant difference in the number of patients with psoriasis resistant to treatment in any psoriatic group ($P>0.3$). Most patients were treated with full dithranol, tar bath, and ultraviolet-light regimen, as advocated by Ingram.[8]

The nail changes which may be very distressing to the patient for cosmetic reasons were resistant to treatment by local applications, but in some patients they underwent complete spontaneous remission. Severe changes were treated with radiotherapy. The lesions resolved but often recurred quickly. In no patients whose nails were treated by radiotherapy did the arthritis of the distal joints remit at the same time.

Often the arthritis was sufficiently mild to require no treatment. This was particularly so in the distal joint group, whose disability was usually minimal. Where therapy was required, a regimen similar to that for rheumatoid arthritis was instituted. Bed rest, salicylate (0.9 gm. every four hours), and appropriate physiotherapy were given in active cases. Twenty-eight patients were given cortisone or prednisolone. There was short-term improvement in the majority, although of four with distal joint arthritis only one improved. Chrysotherapy was given to 48 patients with psoriatic arthritis. Other workers have found a poor response to gold and increased toxicity in these patients.[17] Toxic reactions in the present series were no more frequent (7%) than in 42 of the patients with rheumatoid arthritis who had received gold. A significantly larger proportion of patients with uncomplicated rheumatoid arthritis, however, improved on chrysotherapy than of those with indistinguishable and deforming arthritis.

Differential Agglutination Test (S. C. A. T.)

The S. C. A. T. was done by a modification introduced by Greenbury, Hill, Spalding Smith, and Good.[10] It has been positive in 80% of patients with rheumatoid arthritis and only in a small percentage of non-rheumatoid arthropathies.[10,11] Among the patients with psoriasis and erosive arthritis only 20 had a positive S. C. A. T. Four of these had subcutaneous nodules, and no such nodules were found in those with a negative S. C. A. T. From the point of view of this test alone it is extremely unlikely that if these patients were examples of rheumatoid arthritis with psoriasis a negative result would be obtained in 83% ($P<0.001$).

Comment

The present study provides confirmatory evidence for the tentative suggestion previously made that psoriatic arthritis is a distinct entity.[12] The syndrome is characterized by a negative S. C. A. T., whereas patients with coincidental rheumatoid arthritis and psoriasis have a positive S. C. A. T. The clinical course of the latter patients does not differ from those with uncomplicated rheumatoid arthritis. It is of particular interest that subcutaneous nodules were present in 20%, an incidence similar to that in rheumatoid arthritis,[3,11] since these are regarded as the most characteristic features of the rheumatoid process.[3]

Psoriatic arthritis may be virtually indistinguishable from rheumatoid arthritis

except that the age of onset is earlier, fewer joints are involved, and it is less disabling. It may, however, present primarily as distal joint arthritis closely associated with nail changes, or as a severely deforming type of arthritis. The present paper has been mainly concerned with the dermatological features of these groups.

Some authorities have suggested that the hemolytic Streptococcus is the common etiological agent in psoriasis and its associated arthritis.[18] Figures from this study do not support such a relation. That psoriasis has a marked genetic component is well known and it is probably a modified dominant character.[8] Recent work [19] has confirmed previous indications that there is a hereditary influence in rheumatoid arthritis. The present limited data suggest that in psoriatic arthritis a familial trend exists also.

The age of onset of the psoriasis was similar to that found by other authors.[8] The suggestion of Gribble [20] that in psoriatic arthritis there is a later age of onset could not be confirmed. Only in deforming arthritis was the psoriasis extensive. Contrary to some reports, the soles and palms were not involved more often in psoriatic arthritis, and pustular lesions which have been described as characteristic [15] were only found significantly more often in deforming arthritis.

Various authors have commented on the presence of nail changes in patients with psoriatic arthritis.[5,7] This finding was a feature of the present investigation also, 81% showing nail changes, compared with 32% of the control group with uncomplicated psoriasis. The increased incidence of changes in the control group, compared with other series, probably reflects the older age of the patients. There was a closer association between nail and joint changes than skin and joint lesions. The fact that a high incidence of nail changes was found with coincidental rheumatoid arthritis and psoriasis raises the possibility that such changes may not be specific for psoriatic arthritis but occur with any type of erosive arthritis. In patients with distal joint arthritis, however, the association appeared closer. Nail changes were invariably present, often topographically associated with terminal joint changes and displaying a close clinical correlation with the state of the joint. It has been shown radiographically that not only the distal joints but the tips of the terminal phalanges may be eroded in such patients.[21] The relation of involvement of the teminal phalanges to nail lesions may result from vascular changes, for it is known that similar changes may occur in vascular disorders, such as Raynaud's disease.

Independent treatment of the arthritis and psoriasis on their own merits was required. Experience in the present series was sharply at variance with the suggestion that with adequate treatment of the skin the arthritis will subside.[2] Nor was it found that the psoriasis was more often resistant to treatment in patients with arthritis.[16] Chrysotherapy was no more toxic in psoriatic arthritis than in rheumatoid arthritis but seemed less effective as others have found.[17]

Summary

One hundred fifty-four patients with psoriasis and various rheumatic complaints have been studied. Those with osteoarthritis, gout, rheumatic fever, and muscular rheumatism showed no unusual features of the skin or rheumatic condition and their association seemed fortuitous.

One hundred eighteen patients with psoriasis and erosive arthritis were studied in the light of the sheep cell agglutination test (S. C. A. T.). Twenty with a positive S. C. A. T. were considered to show coincidental psoriasis and rheumatoid arthritis, while the other ninety-eight were thought to be examples of psoriatic arthritis. They were contrasted with control groups of 95 patients with uncomplicated rheumatoid arthritis having a positive S. C. A. T. and 85 patients with uncomplicated psoriasis. Patients with psoriatic arthritis presented with (1) an arthritis similar to rheumatoid

arthritis, (2) primarily a distal joint arthritis, and (3) a severely deforming arthritis. The features of these groups have been analyzed and compared with the control groups of patients.

Prof. S. J. Hartfall extended facilities for this study; Dr. J. T. Ingram allowed me to study many of his patients; the initial work was done with Dr. D. A. Wilkinson and Dr. A. G. S. Hill; Dr. J. Everall assisted in the examination of many of the psoriatic patients.

Department of Medicine, The Johns Hopkins Hospital (5).

REFERENCES

1. Alibert, J. L.: Précis théorique et pratique sur les maladies de la peau, Ed. 2, Paris, Caille et Ravier, 1822.

2. Epstein, E.: Differential Diagnosis of Keratosis Blennorhagica and Psoriatic Arthropathy, Arch. Dermat. & Syph. 40:547, 1939.

3. Short, L. C.; Bauer, W., and Reynolds, W. E.: Rheumatoid Arthritis, Cambridge, Mass., Harvard University Press, 1957, p. 326.

4. Fawcitt, J.: Bone and Joint Changes Associated with Psoriasis, Brit. J. Radiol. 23:440, 1950.

5. Hensch, P. S.: Arthropathica Psoriatica: Presentation of a Case, Proc. Staff Meet. Mayo Clin. 2:89, 1927.

6. Dawson, M. H.: A Note on the Occurrence of Psoriasis in Rheumatoid Arthritis, M. Clin. North America 21:1807, 1937.

7. Sherman, M. S.: Psoriatic Arthritis: Observations on Clinical, Roentgenographic, and Pathologic Changes, J. Bone & Joint Surg. 34A:831, 1952.

8. Ingram, J. T.: The Significance and Management of Psoriasis, Brit. M. J. 2:823, 1954.

9. Chargin, L.: Symposium on the Practical Management of Psoriasis, J. Invest. Dermat. 4:399, 1941.

10. Greenbury, C. L.; Hill, A. G. S.; Spalding Smith, R., and Good, M. S.: The Rose Waaler Test, Lancet 1:554, 1956.

11. Ball, J.: Sheep Cell Agglutination Test for Rheumatoid Arthritis, Ann. Rheumat. Dis. 11:97, 1952.

12. Wright, V.: Psoriasis and Arthritis, Brit. J. Dermat. 69:1, 1957.

13. Empire Rheumatism Council Investigation of Rheumatoid Arthritis, Brit. M. J. 1:799, 1950.

14. Franks, A. G., and Wallace, J. J.: Arthropathic Psoriasis, Mil. Surg. 91:199, 1942.

15. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, Ed. 8, London, Henry Kimpton, 1954, p. 304.

16. MacKenna, R. M. B.: The Problem of Psoriasis, Brit. M. J. 2:207, 1950.

17. Ragan, C., and Tyson, T. L.: Chrysotherapy in Rheumatoid Arthritis: Three-Year Study of 142 Cases, Am. J. Med. 1:252, 1946.

18. Hunt, E.: Psoriasis and Rheumatism: A Comparison, Lancet 2:351, 1933.

19. Lawrence, J. S., and Ball, J.: Genetic Studies on Rheumatoid Arthritis; Ann. Rheumat. Dis. 17:160, 1958.

20. Gribble, M. de G.: Rheumatoid Arthritis and Psoriasis, Ann. Rheumat. Dis. 14:198, 1955.

21. Wright, V.: Psoriasis and Arthritis: A Study of the Radiographic Appearances, Brit. J. Radiol. 30:113, 1957.

Defective Epidermal Utilization and Storage of S^{35} in Psoriasis

MORRIS J. LIPNIK, M.D., and STANLEY H. LEVY, M.D., Detroit

The problem of the etiology and physiochemical mechanism operative in the development of psoriasis has been a stimulant to the efforts of research workers in the field of dermatology. There has been no dearth of work on the part of dermatologists toward attempting to solve the mystery of this disease. In a 10-year period, from 1948-1957, Sulzberger and Baer [1] and Baer and Whitten [2] summarized 86 investigative studies on psoriasis. The great majority of this work has been directed toward methods of therapy and the study of chemical alterations. A summary of the literature of investigative work on psoriasis is to be found in Shelley and Arthur's review.[3] Recently Flesch and Esoda [4,5] reported their studies of the physical and chemical properties of the scales of psoriasis. They were able to find chemical differences unique enough to propose that these differences could form the basis of a specific test for this disease. Their studies demonstrated a chemical defect in the scales, limited to the water-soluble fraction, that consists of an increased sulfhydryl content and a low amino nitrogen content. They also were able to demonstrate an increased amount of pentoses in the scales. Steiner,[6] by histologic methods utilizing differential staining techniques, was able to show that the skin of the psoriatic areas contained large amounts of sulfhydryl and disulfide material throughout the epidermis and particularly in the parakeratotic stratum corneum.

Submitted for publication Dec. 20, 1958.

From the Department of Medicine, Sinai Hospital of Detroit; Section of Dermatology (Dr. Lipnik), and Section of Internal Medicine (Dr. Levy).

To study the metabolic aspects of sulfur compounds in relation to the etiology of psoriasis we used one of the newer investigative modalities, the radioisotope.

A radioisotope of sulfur, incorporated into an essential amino acid, L-methionine, was used in our tests. An in vivo group of tests was performed, with the radioactive sulfur molecule serving as our unit of measurement. The sulfur in L-methionine S^{35} is a pure β-emitter. The presence of the isotope after ingestion could be tracked by counts of its radioactivity. Studies were performed on psoriasis patients and control patients after oral feeding of this tracer compound.

In a previous report we outlined our observations of the skin findings when L-methionine S^{35} is given to psoriatic patients.[7] Our investigations revealed that the diseased skin in a patch of psoriasis was the site of the collection of large quantities of the radioisotopic sulfur. The present study relates our findings with use of S^{35} to study blood peak levels of the radioisotope, urinary and fecal excretion, and comprehensive data on the skin observations of both psoriatic and control patients.

Method and Materials

Nine subjects with psoriasis were tested. They ranged in age from 30 to 64 years. There were four women and five men in the psoriasis test group. All presented a generalized form of psoriasis. To be included in the study they were required to have some plaques of the disease of a minimum diameter of 2.5 cm. None of the patients had exfoliative psoriasis. The nature of their disease process varied from a generalized guttate form of the disease to large confluent plaques of infiltration over sites characteristic of the disease. All of the psoriasis patients tested were outpatients. Four of the group tested were tested prior to any

therapeutic measures aimed at clearing of their disease.

Control patients numbered 14. Their ages ranged from 20 to 69 years. All control patients were completely free of any skin disease. There were three women and eleven men in the control series. The control subjects were tested while they were hospital inpatients.

The radioisotope of sulfur, used as a tracer substance, has the following characteristics: The sulfur was present as S^{35} as part of the molecule of L-methionine. The radioisotope is a pure β-emitter. The β-rays have an intensity of 0.166 mev. The half-life is 87.1 days. It has a specific activity of 27 mc. per gram of methionine.

The patients were given an oral dose of the tracer substance L-methionine S^{35} dissolved in water.[8] Each subject received 40μc. of the tracer substance. The test substance was given at 8 a.m. to the test subjects in the fasting state. They were given a standard meal five hours later. Thereafter, no effort was made to control their dietary intake. Following administration of the tracer substance, tests were performed of the blood, the urine, the feces, and the skin.

The blood was tested to demonstrate positive evidence of gastrointestinal absorption. The time of the peak count was determined and compared with controls. The blood peaks of S^{35} were analyzed by means of venous blood specimens drawn at two-, three-, four-, and five-hour intervals after administration of the test compound. Blood samples of approximately 6 cc. were drawn and placed in oxalated tubes. The blood was then centrifuged. Plasma specimens of 2 cc. volume were pipetted into an open planchet. Counts were done of the plasma in a liquid state. Counts were made for 30 minutes with a TGC-2 thin-walled Geiger tube, under conditions of constant geometry.

Urine specimens were studied in both control and psoriasis patients. The percentage of the oral administered dose recovered in the urine was compared. The urine specimens were collected for 24-hour periods for a total of 72 hours, and the pooled specimens were analyzed. The total volume was determined. A 2 cc. sample of the pooled specimen was pipetted into an open planchet. The readings expressing radioactivity were determined by counting for 30 minutes. The results are expressed as a percentage of the original dose given.

The analysis of fecal specimens was similar to the method outlined for the urinary analysis. The 72-hour pooled specimens were analyzed for S^{35} content. The results are expressed as a percentage of the original oral dose. The method used for examination of fecal specimens is outlined in detail by Sandweiss and Levy.[8]

Counts of the skin were performed with a Geiger tube. A thin-window TGC-2 Geiger tube was employed. All counts listed represent true counts. No corrections were made in any of the counts for the level of radioactive decay. (By actual calculation a slightly higher count would result in the psoriasis patch toward conclusion of the counts than is listed on our data sheet.) The patch to be tested was scanned for five minute periods with the Geiger tube. Constant geometry was used throughout our determinations, with the tube head being placed ⅛ in. from the skin surface. The control subjects' counts were performed on the subscapular area. Psoriasis patients had counts performed on two sites—on both diseased skin and clear skin. The locale for testing clear skin areas was the same as the controls, the subscapular areas. When psoriatic patches were present of adequate size on the back (2.5 cm. or larger) these were the psoriasis test sites. If no psoriasis patches of adequate size were present on the back, other nonhairy sites were used.

To make the test sites as comparable as possible we followed the following routine: The tested sites were cleared of scales daily by light brushing with a tongue-blade applicator, and the same test site was utilized for subsequent testing. The rubbing of the psoriatic patch was necessarily gentle, as we did not want any bleeding in the patch. Test counts of the skin were begun one-half hour after the oral administration of the tracer substance. Then hourly tests were performed for the next five hours. Thereafter the patients returned at 24-hour intervals for repeat tests. The counts were repeated daily for seven days. One patient had test counts performed for nine days. Multiple counts were taken and averaged.

Results

1. Blood Peaks.—The time of blood peak of S^{35} was determined in six of the nine psoriasis patients tested (Table 1). All psoriasis patients tested showed a peak time of absorption of the tracer substance into the blood stream at four hours after oral administration of L-methionine S^{35}. This time is in agreement with the S^{35} blood peak of four hours for normal controls. Twelve of the control subjects (hospital inpatients

TABLE 1.—*Blood Peaks of* S^{35}

	No. Tested	Time of Peak, Hr.
Psoriasis	6	4
Controls		
Outpatient	6	4
Inpatient	10	4
	2	5

TABLE 2.—*Fecal Recovery of* S^{35}

	No. Tested	Recovery, % Average	Range
Psoriasis	6	4.0	2.8-5.2
Control			
Outpatient	24	3.2	0-5.5
Inpatient	13	2.6	0-7.0

free of skin disease) showed results in 10 with a peak of four hours and 2 with a peak of five hours.

II. Fecal Excretion.—The data on fecal excretion, comparing psoriasis patients with controls, are summarized in Table 2. In six of the nine patients with psoriasis, 72-hour stool specimens were analyzed (Table 3). The fecal recovery rate is between the range of 2.8 and 5.2. It is to be noted that the control subjects for fecal excretion are the controls listed by Levy, Sandweiss, Gagliardi, and Feigelson.[9] They list two sets of controls. Normal healthy subjects show an average recovery of 3.2, with a range of 0-5.5, and bedpatients with normal gastrointestinal tracts show an average of 2.6 and a range of 0-7.0. The findings reveal no essential difference between the fecal excretion of S^{35} in patients with psoriasis as compared to controls.

III. Urinary Excretion.—A comparison of the recovery rate in 72-hour urine specimens (urinary excretion) of the psoriasis patients, as compared to controls, reveals little significant difference in the urinary excretion of S^{35}. Psoriasis patients excreted 40% to 60% of the tracer compound, while controls excreted 30% to 60% (Table 4). The excretory amounts of six of nine of the psoriasis patients is listed in Table 3. The average urinary excretion of S^{35} of the psoriasis patient is higher than the controls, 49.2% as opposed to 44.9%, but the difference is not statistically significant.

IV. Epidermal Studies.—The results of skin counts of S^{35} are summarized in Table 5, wherein are listed the average counts of the controls and the psoriatic patients. When the results of psoriatic diseased skin and the two controls of normal skin and psoriatic clear skin are compared, highly significant differences can be seen. By five hours there was a marked variance between these groups; the patches of psoriasis contained over twice the amount of radioactive material as was present in the controls (Fig. 1). The S^{35} counts for the patches of psoriasis continued to increase. They reached their peak by the third to fourth *day*. As the experiments progressed, the psoriatic patches were found to collect two to six times the amount of S^{35} as in the controls (Fig. 2).

Large quantities of the radioactive S^{35} persisted in the psoriatic diseased skin for

TABLE 3.—*Results of Urine, Stool, and Blood Examinations of Psoriasis Patients (6) After Oral Feeding of* L-*Methionine* S^{35}

Patient	Date	Weight, Lb.	Dose, μc.	Radioactivity * 72-Hr. Stool	72-Hr. Urine	72-Hr. Total	Blood Peak, Hr.
1	1/21/58	300	40	3.7	38.0	41.7	4
2	1/30/58	105	40	2.8	53.0	55.8	4
3	2/10/58	153	40	3.8	44.7	48.5	4
4	2/13/58	125	40	3.7	54.4	58.1	4
5	2/24/58	130	40	5.2	46.2	51.4	4
6	3/ 3/58	195	40	4.6	58.3	62.9	4

* Quantity recovered is expressed as a percentage of the original dose.

TABLE 4.—*Urinary Recovery of* S^{35}

	No. Tested	Recovery, % Average	Range
Psoriasis	6	49.2	38.0-58.3
Control	13	44.9	29.2-65.4

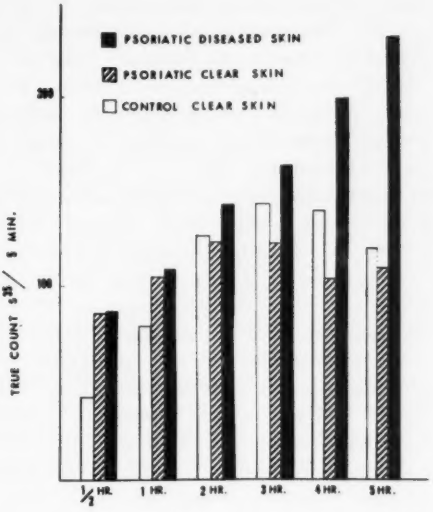


Figure 1

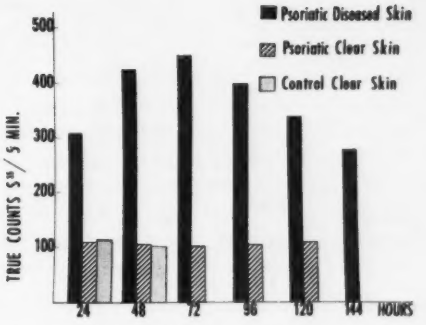


Figure 2

Fig. 1.—Comparison of skin counts (average) of S^{35} of 9 psoriasis patients and 14 control patients without skin disease after oral feeding of L-methionine S^{35}.

Fig. 2.—Comparison (continued from Figure 1) 24 to 144 hours after oral feeding of L-methionine S^{35}. S^{35} skin counts of psoriasis patients (9) and controls (14).

seven days, at which time we concluded our counts. One patient was tested for nine days and found to have significant quantities of the material present nine days after the oral administration of a single tracer dose.

The control patches of (1) normal skin and (2) psoriatic clear skin showed a peak count in three to four *hours*. Moreover, the level of S^{35} of controls is much lower than in the psoriatic patch. Both sets of controls show peak count values that are similar. Most of the radioactive material is eliminated from the normal skin controls by the conclusion of the third day.

The psoriatic clear skin presented some persistence of radioactive material (Table 6) for a longer period. These counts were in the magnitude of one-half to one-sixth of the affected psoriatic patches.

Comment

The findings of our tracer studies demonstrate a striking and, we feel, significant alteration in the patient with psoriasis. This defect concerns the physiochemical handling of compounds containing sulfur. The body defect did not appear to concern either a faulty or increased gastrointestinal absorption or a faulty or increased renal excretion.

TABLE 5.—*Comparison of Average True Skin Counts Every Five Minutes of Nine Psoriasis Patients and Fourteen Controls After Oral Feeding of* L-*Methionine* S^{35}

	Hours					Days					
	½	1	2	3	4	5	2	3	4	5	6	7
Control, Clear skin	45	81	137	147	142	121	111	101	NS *	NS	NS	NS
Psoriasis Clear skin	89	108	132	125	106	112	107	104	99 †	110 ‡	70 ‡	NS
Diseased skin	90	112	147	167	200	235	310	443	450	308	331	284

* Insufficient quantity for measurement.
† 4 of 9 subjects showing residual radioactivity.
‡ 2 of 9 subjects showing residual radioactivity.

TABLE 6.—*Comparison of Residual Radioactivity of Psoriatic Clear Skin and Controls Clear Skin After Single Oral Dose of Forty Microcuries of* L-*Methionine* S^{35}

		No. Showing Residual Radioactivity				
	No. Tested	24-Hr.	48-Hr.	72-Hr.	96-Hr.	120-Hr.
Psoriasis, clear skin	9	8	5	4	2	2
Control, clear skin	14	8	5	0	0	0

What does seem to happen is that in the dynamics of sulfur utilization large quantities of sulfur-containing material seem to accumulate in the skin. The accumulation is continuous, reaching its peak on the fourth day. There seems to be a tendency for the skin of the psoriatic to attract this sulfur, as manifested by the presence of large quantities of the tracer compound as long as nine days after oral ingestion of a single dose of the tracer substance. There should be a rapid utilization of sulfur material in the development of the patches and in the scales because the rate of keratinization is markedly increased in psoriasis. By our mode of testing, where we scraped the scales off of the patches daily and utilized the same area on retesting, significant quantities of the tracer substance should have been eliminated via the scales, but in spite of this daily depletion relatively large quantities of the tracer material persisted in the skin.

Abnormality of Psoriatic Clear Skin

Previous studies have failed to demonstrate any abnormality in the clear skin of the psoriatic. This clear skin possesses the ability to develop new lesions and during certain phases of psoriasis to respond to injury by the development of new lesions at the site of injury (Koebner phenomenon). The tracer study is helpful to determine if there is any abnormality to be found in the psoriatic clear skin. When the data shown in Table 6, dealing with retention of the sulfur isotope in the skin of the control subjects and in the clear skin of patients with psoriasis, are studied, certain differences between these groups can be perceived. The groups apparently differ in the period of retention of the tracer substance. All S^{35} has disappeared from control patients by the third day, while the isotope persists at low levels in some of the psoriatic clear skin. The extreme sensitivity of the tracer study apparently aids in the detection of a difference between these groups. To be of unquestioned statistical validity a much larger sample would be necessary. Does the persistence of S^{35} in psoriatic clear skin demonstrate this potentiality toward disease? The defect in the psoriatic is such that the process of skin repair following injury apparently interferes with the normal function of the cells and some unknown factor in the reparative process following injury apparently catalyzes transformation of the normal tissue into diseased tissue.

Rapidity of Biologic Process

Another aspect of our work should be mentioned. It has been observed by many others working with radioisotopes. That observation concerns the extreme rapidity of the biologic process. Within *one-half hour* after oral feeding of the tracer compound there are present on the skin significant quantities of the tracer substance. The radioisotope is a weak β-emitter; to show radioactivity the sulfur must be in the outermost layer of the skin. From the moment of oral feeding, the tracer element must pass into and be absorbed from the intestinal tract and then pass into the circulatory system. Thence it passes into the lymph system and penetrates into the epidermis. Once in the epidermis it must pass outward, especially through the outer layers of the malpighian layer. Only when it has reached the outermost layers of the epidermis is the tagged sulfur capable of registering its effect on the Geiger tube. Such rapidity of biologic process, where all these steps occur within one-half hour, is amazing. Of practical significance is the application of this data to the psoriatics daily metabolism.

We must assume that, within a short period after ingestion of a protein meal that is the source of sulfur, the sulfur-containing amino acids formed by the hydrolysis of the protein rapidly follow the steps of the radioisotope and are to be found in the skin in the patch of psoriasis, in the increased proportion demonstrated in this study.

Metabolic End-Product of L-Methionine S^{35}

In our studies the metabolic end-product of the tracer compound present in the skin after the oral feeding was not identified. The unit of measurement was the β-ray of the S^{35}. We are fully aware that we are not dealing with elemental sulfur in the patches of psoriatic skin. We do not know whether the S^{35} was present as sulfate, sulfhydryl, disulfide, unchanged methionine, cystine, cysteine, glutathione, or some complex polymerization product of these materials.

Roe [10] has recently shown that one of the proteins present in psoriasis scales was a glucoprotein. By differential staining, a metachromatic material was identified by her to be present in histologic sections of psoriasis. She identifies this material as a polysaccharide, in the nature of chondroitin sulfate, as part of the glucoprotein. The localization of this material was found to be in the intercellular spaces and within the cytoplasm of the parakeratotic cells.

In previous studies with radioisotopes of sulfur, Dziewiatkowski,[11] Böstrom,[12] and Denko and Priest [13] have shown that the uptake of S^{35} varies with the concentration of chondroitin sulfate, the essential polysaccharide of the ground substance. If Roe's work can be confirmed, that an excess of chondroitin sulfate is present in the psoriatic tissue, this could be the cause of the finding that psoriatic tissue is avid in the uptake of the isotopic sulfur. It must be pointed out however, that psoriatic tissue uptake of S^{35} differs from cartilage studies of S^{35} in that the maximum concentration of S^{35} occurs in cartilage in 24 hours while the maximum uptake in psoriatic tissue occurred at 72 to 96 hours.

Enzyme Defect of Psoriasis

There has been considerable evidence presented of enzymatic deficiency that exists in psoriasis, causative of this disease.[3] The enzymatic control of S^{35} deposition has not been mentioned previously in the discussion. In a pertinent study, Böstrom and Månsson [14] demonstrated that the uptake of S^{35} in cartilage was probably enzymatic, by demonstrating that S^{35} was taken up by cartilage suspended in Kreb's solution. In boiled cartilage no similar uptake occurs. They feel that the uptake is mediated by a chondrosulfatase. In their article they point out that other investigators have demonstrated enzymes with sulfatase and chondrosulfatase activity in bacteria and gastropods. There has been no demonstration of these enzymes to exist in the skin in psoriasis lesions.

While no enzymatic determinations were performed in our study, the results point to specific enzymatic defect(s). The interpretation of the regular absorption and retention, forming a smooth digressing biologic curve (Fig. 3), is that a solitary biologic defect or a group of defects, acting simultaneously and continuously, is present in psoriasis. A defect in an enzyme system is one possibility. There may be some as yet unknown enzyme present in normal skin that is defective or hyperactive in psoriasis. The sulfur may be attracted to and combine with some substance present in psoriatic tissue. There could also be extradermal factors producing this defect. The fact that there is a hereditary tendency exhibited in this disease is an additional point in favor of the hypothesis of some enzymatic defect that could be transmitted via genetic pathways.

Therapy and Sulfur Storage Theory

It is interesting that successful therapeutic measures for the treatment of psoriasis are those that are effective in oxidizing, mobilizing, or binding the SH group. The heavy metals, mercury and arsenic, effec-

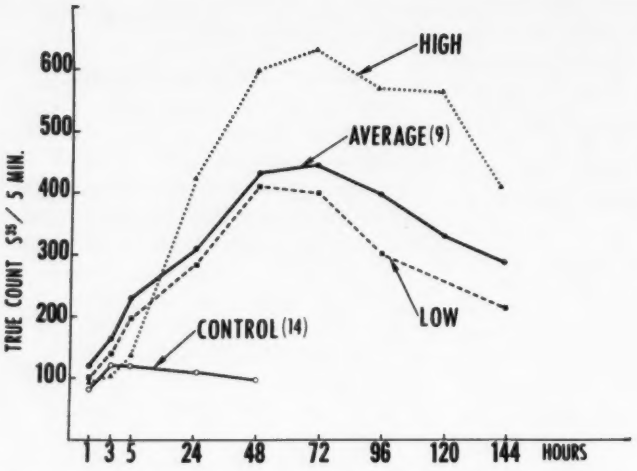


Fig. 3. — Comparative skin counts of S^{35} of 9 psoriasis patients and 14 control patients without skin disease (average counts) after oral feeding of L-methionine S^{35}. Psoriasis counts are shown as the high, low, and average.

tively bind sulfhydryl groups.[15] Cortisone and allied steroid therapy result in an increased excretion by the body of SH groups via increased excretion of the sulfhydryl-containing tripeptide, glutathione.[16] Sunlight apparently affects the sulfhydryl groups by direct oxidation (dehydrogenation). Tars, particularly the crude coal tars that are high in phenolic content, and anthralin and chrysarobin act directly on SH groups because of the oxidizing ability of their OH (hydroxyl) groups. The tars have an additional photosensitizing ability that is of value in promoting oxidation of the sulfur material.

Critical Evaluation

In the evaluation of the data of the epidermal studies the histologic nature of the psoriasis patch must be compared with the controls. Certain critical factors are at variance. First, the elongation of the rete pegs that occurs in psoriasis probably causes only a portion of these pegs to be included in the counts, since the β-ray of sulfur is a weak emitter, with a maximum penetration of 0.8 mm. The counts of psoriatic clear skin and control clear skin are of the entire epidermal layer. Second, there is most likely a difference in the number of cells counted because of the differing histologic architecture, with the controls showing the greater number of cells. Third, the vascularity of the psoriasis area is greater than that of the controls, and the vascular channels are closer to the skin surface. Fourth, the thickened and parakeratotic stratum corneum of the psoriasis patch differs from the corneal surface of the controls.

We are cognizant of the differences outlined above. The factors would seem to favor the controls, as the controls have greater cellularity, more epidermal type cells, and lessened vascularity. The psoriasis patch has the "advantage" of the thickened stratum corneum, yet the rapid keratinization and scale formation should result in using up the stores of the radioisotope and cancel this advantage. Our mode of testing, where we scraped the scales off the lesions daily, should also neutralize this advantage. Yet in spite of these inequities favoring the controls, the psoriasis lesions showed an avid affinity and attractive force, pulling the radioisotope into the skin from body stores of this material.

Summary and Conclusions

A group of 9 patients with generalized psoriasis and 14 control patients free of skin disease were tested for the kinetics of sulfur metabolism by an in vivo method with use of an oral feeding of a labeled essential

amino acid L-methionine S^{35}. Studies, by measurements of radioactivity with the Geiger tube, were performed on the skin, the blood, the urine, and the feces after oral feeding of this sulfur isotope. They indicate that there is no abnormality of either absorption from the intestinal tract and into the bloodstream or excretion via the urine or feces of the labeled sulfur compound by psoriatic patients, as measured by the methods employed. Significant alterations are found in the skin. Psoriatic diseased skin, psoriatic clear skin, and control skin were checked hourly for five hours and subsequently every 24 hours for seven days. Surface counts of the skin, tested by counts of radioactivity with a Geiger counter, showed peak levels of S^{35} were present in controls in four *hours*. Peak levels were present in psoriasis patches in four *days*. There is a quantitative difference at all times with a two- to sixfold increase of the total quantity of S^{35} present in the skin in patches of psoriasis as compared to psoriatic clear skin and normal skin controls. Psoriasis patients show this radiosulfur storage defect for a period of one week after a single dose of the radioactive tracer substance. At the end of one week the psoriatic diseased skin still shows twice as much radioactive sulfur retained as is present at the highest level at any time in controls.

The extreme sensitivity of the isotope study has also demonstrated a difference to exist in psoriatic clear skin. This skin shows a retention of the S^{35} for a longer period than the skin of normal controls.

The causes of this avid retention of sulfur compounds are discussed. This retention appears to be occasioned by a biologic defect or groups of defects acting simultaneously and continuously. Whether this is due to an enzyme system alteration within the patches of the diseased skin is speculative. Successful therapeutic measures in this disease appear related to the ability to bind sulfur material, oxidize this material, or cause increased sulfur excretion.

From our work we propose that there is present in psoriasis a defect in the kinetics of sulfur metabolism relating to the attraction and deposition of sulfur-containing compounds within the skin.

Mrs. Madeline E. Ranney provided technical assistance.

15101 W. Seven Mile Rd. (35).

REFERENCES

1. Sulzberger, M., and Baer, R., Editors: The Year Book of Dermatology and Syphilology (1949-1954), Chicago, The Year Book Publishers, Inc., 1956.

2. Baer, R., and Whitten, V., Editors: The Year Book of Dermatology and Syphilology (1955-1958), Chicago, The Year Book Publishers, Inc., 1958.

3. Shelley, W., and Arthur, R.: Biochemical and Physiological Clues to the Nature of Psoriasis, A. M. A. Arch. Dermat. 78:14 (July) 1958.

4. Flesch, P., and Esoda, E. C. J.: Defective Epidermal Protein Metabolism in Psoriasis, A. M. A. Arch. Dermat. 76:393 (Oct.) 1957.

5. Flesch, P., and Esoda, E. C. J.: Chemical Changes in Psoriatic Scales, Ann. New York Acad. Sc. 73:989 (Nov. 10) 1958.

6. Steiner, K.: Histochemical Observations on Parakeratosis, A. M. A. Arch. Dermat. 77:586 (May) 1958.

7. Lipnik, M., and Levy, S.: To be published.

8. Sandweiss, D., and Levy, S.: Gastrointestinal Absorption with Oleic Acid-I^{131} and L-Methionine-S^{35} in Patients with Ulcerative Colitis, Proc. Soc. Exper. Biol. & Med. 95:259 (June) 1957.

9. Levy, S.; Sandweiss, D.; Gagliardi, R., and Feigelson, H.: To be published.

10. Roe, D.: Application of Paper Electrophoresis to the Diagnosis of Psoriasis: A Study of Psoriatic Scale Extracts, Ann. New York Acad. Sc. 73:977 (Nov. 10) 1958.

11. Dziewiatkowski, D.: Isolation of Chondroitin Sulfate S^{35} from Articular Cartilage of Rats, J. Biol. Chem. 189:187 (Jan.) 1951.

12. Böstrom, H.: On the Metabolism of the Sulfate Group of Chondroitinsulfuric Acid, J. Biol. Chem. 196:477 (June) 1952.

13. Denko, C., and Priest, R.: Distribution of Radiosulfur S^{35}, J. Lab. & Clin. Med. 50:107 (July) 1957.

14. Böstrom, H., and Månsson, B.: On the Enzymatic Exchange of the Sulfate Group of Chondroitinsulfuric Acid in Slices of Cartilage, J. Biol. Chem. 196:483 (June) 1952.

15. Flesch, P., and Esoda, E. J., in Discussion on Flesch, P., and Esoda, E. C. J.[4]

16. Thorn, G. W., et al.: Medical Progress: The Clinical Usefulness of ACTH and Cortisone, New England J. Med. 242:783 (May 18) 1950.

Blood Histamine and Basophil-Eosinophil Counts in Skin Diseases

HERMAN J. SCHULTZ, M.D.; CHARLES F. CODE, M.D., and LOUIS A. BRUNSTING, M.D., Rochester, Minn.

Shortly after histamine was first synthesized by Windaus and Vogt, in 1907,[1] its physiologic properties were described by Dale and Laidlaw,[2] who at the same time called attention to the similarity between the symptoms produced by administration of histamine and those of anaphylaxis. Later, Lewis[3] observed that when stimuli of different kinds were applied to the skin, all elicited a common type of response, which he termed the "triple response." Noting the similarity between that response and histamine-induced wheals, he postulated that the triple response must be due to the liberation by injured cells of a histamine-like substance, which he called "H-substance." Much investigation has ensued in attempts to substantiate histamine as the chemical mediator of anaphylaxis in animals and of allergy in man. Since many dermatologic conditions are partially or totally allergic in origin, estimates have been made of the metabolism of histamine in many of these diseases. Several methods of approach have been utilized, including determination of the histamine content of skin, blood, and urine.

The present study was conceived as an attempt to confirm the results of previous investigators and, if possible, to add to knowledge of the metabolism of histamine in skin diseases. At the same time, it was also hoped that the study might help clarify the question of the carriage of histamine in the blood by the circulating basophils or eosinophils or both.

Submitted for publication Oct. 16, 1958.

Abridgment of thesis submitted by Dr. Schultz to the faculty of the Graduate School of the University of Minnesota, in partial fulfillment of the requirements for the degree of Master of Science in Dermatology.

Fellow in Dermatology (Dr. Schultz), Section of Physiology (Dr. Code), and Section of Dermatology (Dr. Brunsting), Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

Review of the Literature

Previous authors[4-13] have studied the histamine in the blood associated with a variety of skin diseases, particularly urticaria and dermographism; physical allergy, including sensitivity to heat, cold, and irradiation; eczema; neurodermatitis, and postarsenical dermatitis. Their results constitute a potpourri of data; consequently these are not presented in detail. Suffice it to say, however, that the results of previous investigators have been conflicting. Consistent deviations from the normal values for histamine have not been found in the blood of patients with any given disease of the skin.

In 1937, Code[14] raised a basic question from the physiologist's point of view, namely: Is the histamine of blood free in the plasma to produce its physiologic effects, or is it held safely within the cells? That same year, he[14] showed that 70% to 100% of the histamine of whole blood of several species of laboratory animals and of man is contained in the white cells or "buffy coat" of centrifuged blood. The next step was to determine which of the cellular elements of the buffy coat contains the histamine. Code[15] investigated each cell type in the buffy layer to determine its histamine content, and, in his 1952 article,[16] he reviewed in stepwise manner his own work and that of other investigators working on this problem. Only a brief summary will be given here.

Platelets from the blood of human beings, horses, and dogs, obtained by differential

centrifugation, were found to contain negligible amounts of histamine; platelets from rabbits, and perhaps guinea pigs, were exceptions. The lymphoid series of leukocytes were eliminated as histamine carriers by more indirect methods. Normal lymph nodes were found to contain insignificant amounts of histamine. No increase in histamine was found in the blood of patients with lymphatic leukemia or monocytic leukemia, and also only insignificant amounts of histamine were found in monocytic exudates. These observations narrowed the "histamine compartment" of the blood to the granular series of leukocytes.

Greatly increased values for histamine were found in the blood of patients with chronic myelogenous leukemia, and when such patients were given roentgen therapy, a rough parallelism was noted between the decrease in numbers of myeloid cells and the reduction in the amount of histamine in the blood. Myeloblasts were eliminated as the source of this high concentration of histamine when it was noted that the histamine was not increased in acute myelogenous leukemia or in acute exacerbations of chronic myelogenous leukemia. Neutrophils were eliminated on the grounds that histamine is not increased in the blood of patients presenting polymorphonuclear neutrophilic leukocytosis and that no histamine is found in exudates containing large numbers of neutrophils. By exclusion, then, the main carriers of histamine in the blood are thought to be the eosinophils or the basophils or both.

Presently available evidence seems to indicate "In man, both eosinophils and basophils carry histamine; the load per basophil seems quite fixed, while that in the eosinophil is variable."[17] This statement is supported by several observations. Code and Mitchell[18] found that administration of cortisone to adrenalectomized dogs and to healthy men produced a parallel reduction in both histamine and the number of eosinophils in the circulating blood. Later, Code and associates[19] again administered cortisone to healthy men, and Osada[20] administered corticotropin (ACTH); in both instances, parallel reduction was found in the number of circulating basophils and eosinophils. A close relationship between these two types of cells was further supported by Hamerston and co-workers,[21] who found a significant correlation between the absolute basophil and eosinophil counts in blood from a group of institutionalized human subjects. Separating the various types of blood cells by special centrifugation techniques, Graham and co-workers[22] found that about half of the histamine content of normal blood is in the basophils; a third is in the eosinophils, and the remaining sixth is in all the other blood elements combined.

Rose,[23] on the other hand, stated that histamine is probably *not* carried by eosinophils, and Valentine and co-workers,[24] studying patients with chronic granulocytic leukemia, found a positive correlation between histamine in the blood and the number of basophils and a negative correlation between histamine and the other myeloid elements of the blood. Valentine[25] concluded, "Available data fail to indicate that the eosinophil has any special importance in histamine metabolism."

In some of their studies of histamine in the blood of patients with dermatologic conditions, Rose[12] and Nilzén[9,10] attempted to correlate changes in blood histamine with fluctuations in numbers of circulating eosinophils but found no invariable parallelism.

Methods and Procedures

In general, patients selected had dermatoses known to be associated with blood eosinophilia or tissue eosinophilia. Other criteria were tissue basophilia and bona fide reactions of hypersensitivity. Some dermatoses of miscellaneous types also were included.

A total of 36 patients with dermatoses of moderate to severe degree were studied. Most of the patients were hospitalized during the period of the study. All of the patients were treated topically with standard dermatologic medicaments. When more specific or systemic therapy was used, it will be indicated in the presentation of the data obtained from individual patients. In some instances, systemic antihistaminic therapy had been given to a patient prior to the time that the study was begun.

In such cases, use of this medication was discontinued for a minimum of 24 hours and in most such instances for several days to weeks prior to drawing blood for this study. Similarly, when steroid therapy had been utilized, the investigation was postponed until such medication had been discontinued for a minimum of two weeks.

Each study consisted of determination of the number of eosinophils and basophils and the concentration of histamine in each specimen of blood. Chamber methods of counting the eosinophils and basophils were used. For counting eosinophils, the diluting fluid used was that recommended by Randolph,[26] a phloxine-propylene glycol aqueous stain. The basophils were enumerated according to the technique of Moore and James,[27] with the aid of a toluidine blue stain. Determinations of histamine were done by the Code modification of the Barsoum and Gaddum method.[28] The term "blood histamine," as herein used, indicates the active substance responsible for contracting the ileum of the guinea pig after extraction from the blood by Code's method. The concentrations are expressed as micrograms of histamine base per milliliter of blood.

Whenever possible, blood was withdrawn for two or more sets of determinations on each patient. The terms "early" and "late" are used to relate the time of the test to the time that the patient was under our care.

Normal or control values for the three variables are well documented by previous workers. Moore and James[27] found that the range of circulating basophils in males was 11 to 107 per cubic millimeter of blood, with a mean of 46.7; in females, the range was 8 to 88 with a mean of 40.6. Sturgis[29] quoted several authors' figures for normal eosinophil counts but finally seemed to accept the normal range of 25 to 300. Code[16] stated that the normal value for histamine in the blood of man is 0.02μg. to 0.08μg. per milliliter, expressed as histamine base. Experience in our laboratory has led to the view that values of more than 0.06μg. per milliliter should be regarded as suspiciously high and those of more than 0.08μg. may be considered abnormal. Our experience and that of others have revealed also that, when blood is drawn repeatedly from a healthy person under standard conditions, the degree of variability is minimal.

Comment should be made regarding the points of differential diagnosis used to categorize patients with atopic dermatitis, neurodermatitis, and sensitization secondary to neurodermatitis. In general, the criteria for the diagnosis of atopic dermatitis employed were those enumerated recently in the monograph of Baer and collaborators.[30] Briefly, such patients are children or young adults who present a chronic lichenified dermatitis favoring the flexural regions and who usually exhibit white dermographism; in addition, these patients usually have additional personal manifestations of atopy or a family background of atopy or both. The term "neurodermatitis" is applied to forms of eczema, generally chronic, in which no specific etiologic factor can be elicited. For the most part, neurodermatitis appears in older persons who present either localized, usually multiple, patches or a generalized eruption of eczematous dermatitis, often lichenified. Sensitization secondary to neurodermatitis, as the term implies, indicates a reaction or allergic response of the eczematous skin to some chemical insult, internal or external.

Results

Atopic Dermatitis (Table 1).—The ages of the nine patients with this condition in the series ranged from 12 to 56 years, and the duration of dermatosis, from 1½ to 49 years. The mean early and late basophil counts (both 57 per cubic millimeter) were within the normal range, although higher than the usual mean normal value for basophils. The mean eosinophil counts were 1,005 early and 834 late; both were mark-

TABLE 1.—*Results of Blood Studies in Nine Cases of Atopic Dermatitis*

		Basophils/Cu. Mm.		Eosinophils/Cu. Mm.		Histamine, μg/Ml.	
Age, Yr.	Sex	Early	Late	Early	Late	Early	Late
56	M	43	50	781	438	0.058	0.050
15	M	56	50	1,112	869	0.100	0.095
			72		1,013		0.124
12	M	78	46	544	708	0.114	0.089
15	M	60	110	1,644	1,713	0.124	0.133
26	M	50	41	1,531	844	0.057	0.040
23	M	56	31	594	388	0.058	0.049
17	M	56	56	831	731	0.102	0.053
23	M		59		413		0.049
18	M		53		1,225		0.091
Mean		57	57	1,005	834	0.088	0.077

TABLE 2.—*Results of Blood Studies in Five Cases of Neurodermatitis*

		Basophils/Cu. Mm.		Eosinophils/Cu. Mm.		Histamine, μg/Ml.	
Age, Yr.	Sex	Early	Late	Early	Late	Early	Late
43	M	89	106	1,656	806	0.133	0.147
			88		1,131		0.133
52	M	63	66	213	206	0.089	0.089
27	F	50	47	419	575	0.057	0.059
37	M		22		100		0.032
43	M		38		650		0.044
Mean		67	61	763	578	0.093	0.084

edly elevated. Also, all patients individually showed consistently elevated eosinophil counts. The mean concentrations of histamine in the blood (early 0.088μg. and late 0.077μg. per milliliter) were in the top normal or "borderline elevated" range. The histamine content of the blood of four of the nine patients exceeded the upper limit of normal before treatment, and it declined to the normal range on treatment in one of the four patients. No consistent relationship was noted between changes in any of the three variables studied and the clinical course of the patients during treatment.

Neurodermatitis (Table 2).—Five patients were studied; their ages ranged from 27 to 52 years, and the duration of dermatosis, from 4 to 32 years. The mean basophil counts (67 early and 61 late) were within the normal range, although higher than the mean normal value. The mean eosinophil counts (763 early and 578 late) were moderately elevated. The mean concentrations of histamine in the blood (0.093μg. early and 0.084μg. late) were in the "borderline elevated" range. The histamine content of the blood of two of the five patients exceeded the upper limit of normal early, and it did not decline to the normal range with treatment. No consistent relationship was noted between changes in any of the three variables studied and the clinical course of the patients during treatment.

Sensitization Secondary to Neurodermatitis (Table 3).—Five patients were studied, ranging in age from 52 to 76 years. The localized skin eruption ranged in duration from 1½ months to 39 years, while the generalized sensitization eruption ranged in duration from two weeks to two to three months. The mean basophil counts (33 early and 48 late) were within the normal range. In all of the patients, however, the basophil count increased in the course of treatment. The mean early eosinophil count (474) was only slightly above normal, while the mean late count (1,113) was markedly elevated. No *consistent* changes in the eosinophil counts of the individual patients were noted in the course of treatment. The mean concentrations of histamine (0.052μg. early and 0.070μg. late) were normal. The concentration of histamine in the blood of three of

TABLE 3.—*Results of Blood Studies in Five Cases of Sensitization Secondary to Neurodermatitis*

		Basophils/Cu. Mm.		Eosinophils/Cu. Mm.		Histamine, μg/Ml.	
Age, Yr.	Sex	Early	Late	Early	Late	Early	Late
76	M	31	47	856	2,738	0.040	0.062
			16		2,475		0.065
55	M	44	63	756	588	0.074	0.084
74	M	34	69	600	700	0.051	0.084
55	F	13	16	13	6	0.018	0.022
52	M	41	78	144	169	0.077	0.100
Mean		33	48	474	1,113	0.052	0.070

TABLE 4.—*Results of Blood Studies in Seventeen Cases, Representing Twelve Miscellaneous Dermatoses*

		Basophils/Cu. Mm.		Eosinophils/Cu. Mm.		Histamine, μg/Ml.	
Age, Yr.	Sex	Early	Late	Early	Late	Early	Late
			Mycosis Fungoides				
68	M		122		163		0.100
77	M	*		25		0.067	
		66 †	16 ‡	31 †	6 ‡	0.072 †	0.023 ‡
46	M		34		225		0.047
Mean		66	78 §	28	194 §	0.070	0.074 §
			Pemphigus Vulgaris				
79	M	38	50	188	175	0.037	0.050
		28	*	125	238	0.031	0.044
Mean		33	50	157	207	0.034	0.047
			Urticaria Pigmentosa				
41	F	44	53 #	256	281 #	0.056	0.069 #
73	M	6	9 #	6	6 #	0.027	0.033 #
Mean		25	31	131	144	0.042	0.051
			Chronic Urticaria				
42	M	16		231		0.032	
62	F		3		63		0.009
			Dermatitis Herpetiformis				
37	F	53	41 ¶	263	213 ¶	0.056	0.050 ¶
55	M	28		400		0.044	
Mean		41	41	332	213	0.050	0.050
			Dermatomyositis				
38	F	50		238		0.049	
			Epidermolysis Bullosa				
7	F	28		269		0.034	
			Erythema Multiforme				
31	F	34		193		0.045	
			Erythroderma of Undetermined Etiology				
51	M	163	150	3,313	1,244	0.200	0.200
			157		1,575		0.210
			Pemphigus Foliaceus				
45	M	28	19	144	69	0.035	0.027
			Primary Systematized Amyloidosis				
58	M	34		69		0.047	
			Prurigo Nodularis				
43	F	41		925		0.069	

* Specimen lost.
† Immediately prior to intravenous injection of corticotropin.
‡ 1 hr. after 8-hr. intravenous infusion containing 20 units of corticotropin.
§ Value obtained after injection of corticotropin was not used in calculating these means.
# After a 15-min. hot bath.
¶ 2 days after treatment with sulfapyridine was started.

the five patients was at some time in the study above the normal range. In addition, the concentration of histamine in the blood of all of the patients consistently increased during treatment.

Miscellaneous Dermatoses.—Data on the remainder of the patients, numbering 17, and representing 12 dermatoses are presented in Table 4. A few of these require further comment.

In one patient with mycosis fungoides a study was made immediately prior to and one hour after an eight-hour intravenous infusion of 20 units of corticotropin in 1,000 ml. of 5% solution of dextrose in distilled water. A parallel decrease in basophils, eosinophils, and histamine was observed.

In both of the patients with urticaria pigmentosa it was recognized that increased itching and urtication followed a hot bath. In view of this, the samples of blood were drawn before and after such stimulation. Both patients had a minimal increase in each of the three variables studied, 15 minutes after a hot bath.

The highest basophil count, eosinophil count, and values for histamine in the blood in the entire study were observed in the patient who was given a diagnosis of "erythroderma of undetermined origin." The possibility of lymphoblastoma had been raised clinically about this patient's condition; however, the laboratory studies did not substantiate that possibility, the only abnormalities being anemia and azotemia.

TABLE 5.—*Analysis of Blister Fluid of the Patient with Pemphigus Vulgaris*

Time of Test	Basophils/ Cu. Mm.	Eosinophils/ Cu. Mm.	Histamine in Blister Fluid, μg/Ml. Total	Supernatant	Cells
Early	69	731	0.041		
	13	431	0.029		
Mean	41	581	0.035		
Late	13	244	0.016		
	6	163	0.011	0.005	0.010
	38	225	0.057	0.007	0.040
Mean	19	211	0.028	0.006	0.025

In the patient with pemphigus vulgaris, examinations of the blister fluid were performed simultaneously with the examinations of the blood. The results are presented in Table 5. By careful separation of the supernatant fluid from the sediment following centrifugation, it was observed that the histamine of the blister fluid was apparently confined to the cellular elements of the fluid rather than free in the liquid medium, thus showing a situation parallel to that found in the blood.

Statistical Comparisons of the Three Variables Studied.—In order to evaluate possible relationships between the three variables studied, the data were plotted graphically and correlation coefficients were

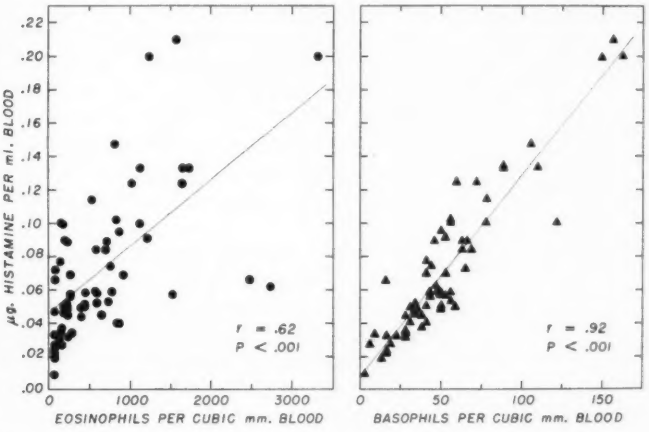


Fig. 1.—Relationship in the number of eosinophils and basophils to the concentration of histamine in the blood of 36 patients with skin diseases of various types.

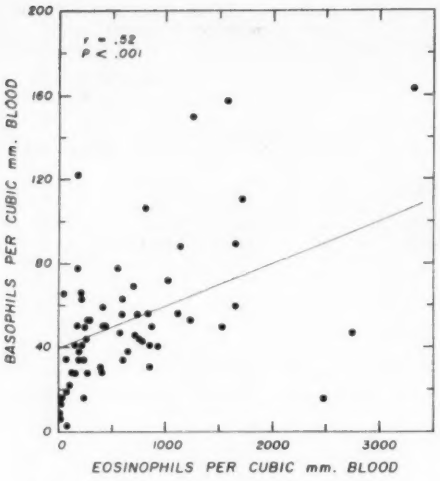


Fig. 2.—Relationship between the number of basophils and of eosinophils in the blood of 36 patients with skin diseases of various types.

calculated between (1) the basophil counts and the concentrations of histamine, (2) the eosinophil counts and the concentrations of histamine, and (3) the basophil counts and the eosinophil counts. The results are shown in Figures 1 and 2.

A definite and consistent numerical relationship between the numbers of circulating basophils and the levels of histamine in the blood is indicated by the correlation coefficient of 0.92. A significant, although not as clear-cut, correlation was found between the numbers of circulating eosinophils and the levels of histamine, with a correlation coefficient of 0.62; thus, a less consistent or more variable numerical relationship is indicated between these two factors. Search for a relation between the numbers of circulating basophils and circulating eosinophils revealed a correlation coefficient of 0.52; thus, in the patients with the various diseases we studied, the numbers of cells of these two types were not closely related.

Comment

Fluctuations in the histamine values in the blood observed in serial examinations of many of the individual patients studied, when compared to the *constant* day-to-day values for histamine in the blood of control subjects, suggest some degree of alteration of the histamine metabolism in these patients. This statement is also supported by the observation that the concentration of histamine in the blood of 12 of the 36 patients was at some time in the study above the normal range.

In general, basophil counts and levels of histamine fluctuated in parallel. Changes in eosinophil counts, however, were inconsistently related to changes in the other two factors.

In the group of dermatoses studied, deviation from the normal number of circulating basophils and concentration of histamine in the blood was not consistent. In patients with atopic dermatitis and neurodermatitis, however, the data allow the conclusion that the metabolism of histamine is often disturbed in such a fashion that elevated blood levels of histamine are found. In no case were these levels diminished.

In patients with sensitization secondary to neurodermatitis, a consistent increase in the number of basophils as well as in the concentration of histamine in the blood was noted in the course of treatment. In the other dermatoses studied, clinical improvement was not accompanied by changes in these two factors.

In all patients with atopic dermatitis, as well as in the majority of patients with neurodermatitis and sensitization secondary to neurodermatitis, eosinophil counts were elevated. In the remainder of the dermatoses studied, however, these counts were variable. In the entire group, no relationship between changes in the number of circulating eosinophils and the clinical course of the patients was observed.

A definite and consistent relationship was found in our patients between the number of circulating basophils and the concentration of histamine in the blood, as well as a more variable relationship between the number of circulating eosinophils and the amount of histamine in the blood. A similar situa-

tion obtains in healthy persons.[17] The consistency of the relationship between the number of circulating basophils and the amount of histamine in the blood indicates that the basophils in the disease conditions which we studied carry a fixed amount of histamine per basophil, as they have been found to do in healthy persons.[17] Although the number of basophils and the number of eosinophils in the blood of the patients we studied are somewhat related, the correlation is in no way as definite as that encountered in healthy persons.[19-21] The lack of a fixed relationship between the numbers of these two types of cells may be the result of some fundamental derangement in the diseases we studied. The variability in the concentration of histamine in the blood of the patients, which was another striking abnormality, also may be related to such a derangement.

Summary

This study was undertaken to answer certain questions relating to the metabolism of histamine. Do significant changes in concentration of histamine in the blood occur in patients with certain skin diseases, particularly those associated with itching and eosinophilia? Could such changes in concentration of histamine in the blood be related to the number of circulating eosinophils or basophils or both? Could measurement of these three factors in such patients, followed by statistical comparisons, help clarify the question of the transport of histamine?

One or more samples of blood were taken from 36 patients who had 15 diseases of the skin, predominantly atopic dermatitis and neurodermatitis. Each sample of blood was examined simultaneously for concentration of histamine and numbers of basophils and eosinophils. The data were plotted graphically and correlation coefficients were calculated.

The evidence indicates some degree of alteration of the metabolism of histamine in these patients. This is supported primarily by the observation that the concentration of histamine in the blood of 12 of the 36 patients was at some time in the study above the normal range and that patients followed serially showed marked and unpredictable fluctuation in concentration of histamine, in comparison to the constant day-to-day levels known to occur in normal persons.

Statistical comparisons of the three factors studied offer support to the thesis that basophils are the most consistent carriers of histamine in the blood of human beings and that eosinophils serve in this capacity in a more variable manner.

Mayo Clinic.

REFERENCES

1. Windaus and Vogt, cited by Dale.[2]

2. Dale, H. H., and Laidlaw, P. P.: The Physiological Action of β-Iminazolylethylamine, J. Physiol. 41:318-344 (Dec. 31) 1910.

3. Lewis, T.: The Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, 1927.

4. Capps, R. B., and Young, R. H.: Hypersensitivity to Light: Studies on an Unusual Case Treated Successfully with Histamine, J. Clin. Invest. 19:778-779 (Sept.) 1940.

5. Cerqua, S., cited by Rose.[12]

6. El-Sayed, M. F. A.: Estimation of Blood Histamine in Allergic Skin Diseases, J. Roy. Egyptian M. A. 33:810-818, 1950.

7. Gate, J.; Pellerat, J.; Badel, M., and Murat, M.: Recherches sur l'histaminémie: L'Histaminurie en dermatologie et le taux physiologique de l'histamine cutanée, Compt. rend. Soc. biol. 138:542-544 (Jan. 17) 1944.

8. Mitumoto, S.: Histamingehalt im Blut und Harn bei Hautkrankheiten, Jap. J. Dermat. & Urol. 49:25-26 (March 20) 1941.

9. Nilzén, A.: Studies in Histamine (H-Substance) with Special Reference to the Conditions Obtaining in Urticaria and Related Skin-Changes, Acta dermat.-venereol. (Supp. 17) 27:1-68, 1947.

10. Nilzén, A.: Blood Histamine and Arsphenamine Dermatitis, Acta dermat.-venereol. 27:521-527, 1947.

11. Rose, B.: Studies on Blood Histamine in Cases of Allergy: I. Blood Histamine During Wheal Formation, J. Allergy 12:327-334 (May) 1941.

12. Rose, B.: Studies of Blood Histamine in Patients with Allergy: II. Alterations in the Blood Histamine in Patients with Allergic Disease, J. Clin. Invest. 20:419-428 (July) 1941.

13. Tarras-Wahlberg, B.: Blood Histamine in Salvarsan-Dermatitis, Acta dermat.-venereol. 18: 284-292 (June) 1937.

14. Code, C. F.: The Source in Blood of the Histamine-like Constituent, J. Physiol. 90:349-364 (Aug.) 1937.

15. Code, C. F.: The Histamine-like Activity of White Blood Cells, J. Physiol. 90:485-500 (Sept.) 1937.

16. Code, C. F.: Histamine in Blood, Physiol. Rev. 32:47-65 (Jan.) 1952.

17. Code, C. F.: Discussion, in Ciba Foundation Symposium Jointly with the Physiological Society and the British Pharmacological Society on Histamine, edited by G. E. W. Wolstenholme and C. O'Conner, Boston, Little, Brown & Company, 1956, pp. 412-413.

18. Code, C. F., and Mitchell, R. G.: Cited by Code.[17]

19. Code, C. F.; Mitchell, R. G., and Kennedy, J. C.: The Effect of Cortisone on the Number of Circulating Basophils and Eosinophils: Is There a Relationship Between These Cells? Proc. Staff Meet. Mayo Clin. 29:200-204 (April 7) 1954.

20. Osada, Y.: Parallel Changes in the Numbers of Circulating Eosinophils and Basophils Induced by ACTH Administration, Bull. Inst. Publ. Hlth., Tokyo 4:12-18 (Sept.) 1954.

21. Hamerston, O.; Elveback, L.; Halberg, F., and Gully, R. J.: Correlation of Absolute Basophil and Eosinophil Counts in Blood from Institutionalized Human Subjects, J. Appl. Physiol. 9:205-207 (Sept.) 1956.

22. Graham, H. T.; Lowry, O. H.; Wheelwright, F.; Lenz, M. A., and Parish, H. H., Jr.: Distribution of Histamine Among Leukocytes and Platelets, Blood 10:467-481 (May) 1955.

23. Rose, B.: Histamine, Hormones and Hypersensitivity, in Recent Progress in Hormone Research, edited by G. Pincus, New York, Academic Press, Inc., Vol. 7, 1952, p. 377.

24. Valentine, W. N.; Lawrence, J. S.; Pearce, M. L., and Beck, W. S.: The Relationship of the Basophil to Blood Histamine in Man, Blood 10:154-159 (Feb.) 1955.

25. Valentine, W. N.: The Enzymes of Leukocytes, Ann. New York Acad. Sc. 59:1003-1011 (March) 1955.

26. Randolph, T. G.: Blood Studies in Allergy: I. The Direct Counting Chamber Determination of Eosinophils by Propylene Glycol Aqueous Stains, J. Allergy 15:89-96 (March) 1944.

27. Moore, J. E., III, and James, G. W., III: A Simple Direct Method for Absolute Basophil Leukocyte Count, Proc. Soc. Exper. Biol. & Med. 82:601-603 (April) 1953.

28. Code, C. F.: The Quantitative Estimation of Histamine in the Blood, J. Physiol. 89:257-268 (April) 1937.

29. Sturgis, C. C.: Hematology, Ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1955, p. 734.

30. Baer, R. L.: Atopic Dermatitis, Philadelphia, J. B. Lippincott Company, 1955.

Investigations on the Effect of Psoralen Derivatives on Blood Sugar and Glutathione

ANWAR EL-MOFTY, M.D.; ABDEL MONEM EL-MOFTY, M.D.; HASSAN ABDELAL, D.V.D., and M. F. S. EL-HAWARY, Ph.D. (London), Cairo, Egypt

Since 1948, new drugs, psoralens (Ammoidin and Ammidin, which are 8-methoxypsoralen and 5-isoamyleneoxypsoralen, respectively), separated in crystalline form from the extracts of the fruits of an Egyptian herb, Ammi majus linn,[1] have been used with success by one of us (A. M. E-M.) in 1948 [2,3] and 1949 in the treatment of leukoderma. Since then, many investigators [4-6] have tried these drugs in the treatment of leukoderma, and they have confirmed its successful results.

In our trials on these drugs for the last 10 years we were fully aware of the importance of detecting and reporting any undesirable side-effects.

The possibility of a potential danger of aggravating a diabetic process was raised when one of us (A. M. E-M., 1952 [8]) reported two cases of mild diabetes where a possible aggravation of their diabetes was clinically suspected. One of these cases was a dentist, treating himself by using 800 mg. of Ammoidin daily (10 times the recommended dose) over a period of three days. He claimed to have developed diabetes immediately after taking the drug. These observations were taken seriously, and it was advised that the drug should not be given to diabetic leukodermic patients.

On the other hand, all patients receiving the drug were followed up for detection of early evidence of diabetes all through the duration of treatment. No case developed diabetes under psoralen treatment, which was carried up to two years in some patients.

When we were confident that the drug did not induce a diabetic state, and before using it in patients already with diabetes, it was thought advisable to carry on some animal experiments, studying their blood sugar levels under higher doses of psoralen compounds to settle the question.

Again the apparent similarity between the chemical structure of psoralen and alloxan (the most potent experimental diabetogenic agent) made these experiments necessary. As it was suggested that the similarity in structure is due to the occurrence of an active ketogroup (C=O) in both and as the reaction of this ketogroup with the SH-group of tissues was thought to be the explanation of the diabetogenic effect of alloxan [7] causing depletion of SH-group of tissues, it was held advisable to study the behavior of SH-group in tissues and blood of experimental animals receiving psoralens. The structures of alloxan and the psoralen compounds are shown in Figure 1.

Experimental

Albino rats weighing from 100 to 200 gm. were used. Ammoidin or Ammidin was tried separately or in a mixture of both either in acute or chronic experimentation. The drugs were given to rats in

Submitted for publication July 28, 1958.

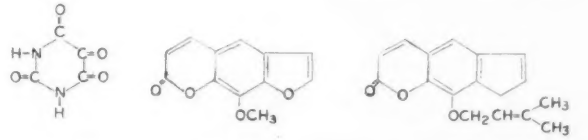


Fig. 1.—Chemical structure of alloxan, Ammoidin, and Ammidin.

TABLE 1.—*The Effect of the Administration of Psoralen Compounds* *

Rat No.	Bl. S. B. †, Mg. %	Bl. S. A. ‡, Mg. %	Experiment
1	100	104	Rats receiving Ammoidin, 400 mg/kg. body weight, orally mixed with food; killed 48 hr. after administration
2	87	84	
3	80	78	
4	75	80	Rats receiving Ammidin, 400 mg/kg. body weight, orally mixed with food; killed 48 hr. after administration
5	100	90	
6	95	90	
7	75	80	Rats receiving 200 mg. Ammoidin and 200 mg. Ammidin/kg. body weight, orally mixed with food; killed 48 hr. after administration
8	95	90	
9	90	97	
10	110	112	Rats receiving 800 mg. Ammoidin/kg. body weight, orally mixed with food; killed 48 hr. after administration
11	80	90	
12	107	110	
13	70	66	Rats receiving Ammidin, 800 mg/kg. body weight; killed 48 hr. after administration
14	83	80	
15	70	74	Rats receiving 400 mg. Ammoidin and 400 Ammidin/kg. body weight, killed 48 hr. after administration
16	81	72	
17	67	72	
18	110	112	Rats receiving 100 mg. Ammoidin with 100 mg. Ammidin/kg. body weight over period of 4 days
19	80	90	
20	107	110	

* This table shows clearly that there is no change in the blood sugar levels after the administration of psoralen derivatives.
† Bl. S. B. indicates blood sugar before the administration of the drug.
‡ Bl. S. A. indicates blood sugar after the experimentation period.

doses of 200, 400, and 800 mg. per kilogram of body weight orally mixed with food given by force feeding with a polyethylene (Polythene) tube attached to a syringe. The blood was drained from the tail of the rats both before and after experimentation. In experiments to study the effect of psoralens on the blood glutathione levels the rats were given doses of 800 mg. per kilogram of body weight of Ammoidin and/or Ammidin and the animals killed 24-48 hours after the administration of the drug.

Methods

For blood sugar, the method of Haselwood and Strocksan for the estimation of true glucose in blood was used,[11] and for the estimation of blood glutathione, the method of Thompson and Watson, 1952,[12] was used.

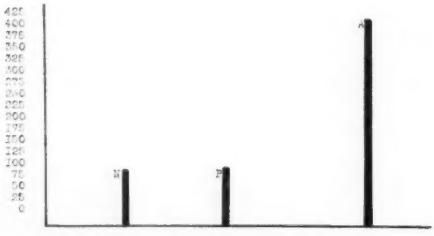


Fig. 2.—*N*, normal blood sugar level in milligrams per cent of glucose. *P*, blood sugar levels in animals treated with Ammoidin and Ammidin in doses of 200, 400, and 800 mg. per kilograms of body weight.

Results

The results obtained for blood sugar are summarized and graphically represented in Figure 2.

The animals used for the study of the effect of psoralen compounds on the level of blood glutathione were given doses of 800 mg. of either Ammoidin or Ammidin per kilogram of body weight and killed 24-48 hours later. The results obtained for blood glutathione are given in Table 2.

The level of glutathione in rats receiving no drugs, i. e., normal rats, is found to be 21.2, 22.2, 23.5, 26.8, 24.6, and 24.3, with a mean of 23.8 mg. %. These results show that, although the mean values are not far from each other as compared to the normal

TABLE 2.—*Results for Blood Glutathione* *

Rat No.	Blood Glutathione	
	Ammoidin	Ammidin
1	24	16.8
2	15.2	21.2
3	24.5	21.2
4	20.2	
5	26.4	
6	26.6	
7	16.8	
Mean	20.4	19.8

* Mg/100 ml. blood.

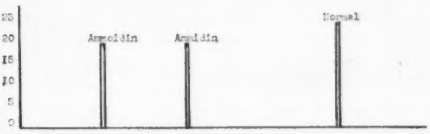


Fig. 3.—Blood glutathione, mean levels in normal and Ammoidin- and Ammidin-treated animals expressed as by milligrams per 100 ml. of blood.

mean, some values for the blood glutathione in the Ammoidin- and the Ammidin-treated rats with doses of 800 mg. per kilogram of body weight are slightly lower than the normal values obtained for blood glutathione of normal rats. The results obtained for blood glutathione in the normal and Ammoidin- and Ammidin-treated rats are represented in Figure 3.

Comment

As it is reported by El-Mofty, in 1952,[3] that one case of diabetes responded unfavorably to psoralens by aggravating the diabetic condition and increasing the demand for insulin, it has been held since that time that diabetes is a contraindication to the use of the drugs.

When it was postulated by Lerner et al.[7] (1953) that there is partial similarity between psoralens and alloxan in structure and that both may react with sulfydryl groups, the rigid contraindication of psoralens in diabetes seemed to be finally established.

Yet through our prolonged experience with psoralens we have never met with any patient who has developed diabetes or has shown a diminished sugar tolerance. In the present series of experiments it has been shown that in both acute and chronic experiments no change in blood sugar occurred although the dose used in the present work is far greater than the dose of alloxan which causes the appearance of diabetes in rats (M. F. S. E-H., 1955.[10])

In a parallel series of experiments it was also observed that no appreciable change in the sulfydryl content in the blood (as estimated as glutathione) occurred.

These results are conclusive that psoralens have neither diabetogenic effect nor any considerable effect on the glutathione levels in blood of rats.

Summary

Ammoidin (8-methoxypsoralen) and Ammidin (5-isoamyleneoxypsoralen) have been found to cause no variation in the levels of blood sugar and glutathione when given in doses of 200, 400, and 800 mg. per kilogram of body weight in acute experimentation. Also, the two drugs were found to be of no effect on the blood of two constituents analyzed when given to rats in doses of 100 mg. per kilogram of body weight in chronic experimentation. It has been shown that the similarity to alloxan in structure does not parallel its diabetogenic effect. It is concluded, thus, that the psoralen compounds can be given safely to normal as well as to diabetic persons.

This work comprises steps in the series of investigations of the problem of the treatment of vitiligo by psoralen compounds—the crystalline extracts of an Egyptian herb, Ammi majus linn—originally started and supervised by Dr. Abdel Monem El-Mofty. The crystalline Ammoidin and Ammidin are manufactured and supplied by Memphis Chemical Co., Cairo.

71 Nubar St., Falaky Sq. (Dr. El-Mofty).

REFERENCES

1. Fahmy, I. R., and Abu Shady, H.: Quart. J. Pharm. & Pharmacol. 21:499, 1948.

2. El-Mofty, A. M.: J. Roy. Egyptian M. A. 31:651, 1948.

3. El-Mofty, A. M.: J. Roy. Egyptian M. A. 35:1, 1952.

4. Sheldon, S. A.; Harrel, E. R., and Cutis, A. C.: A. M. A. Arch. Dermat. 74:9, 1955.

5. Sidi, E., and Bourgeois-Gavardin, J.: Presse méd. 61:436, 1953.

6. Couperus, M.: California Med. 81:402-406, 1954.

7. Lerner, A. B.; Denton, C. A., and Fitzpatrick, T. B.: J. Invest. Dermat. 20:299, 1953.

8. El-Mofty, A. M.: Brit. J. Dermat. 64:431, 1952.

9. Lazarow, A.: Physiol. Rev. 29:48, 1949.

10. El-Hawary, M. F. S.: Biochem. J. 61:348-352, 1955.

11. Haselwood, G. A. D., and Strockman, T. A.: Biochem. J. 33:920, 1939.

12. Thompson, R. H. S., and Watson, D.: J. Clin. Path. 5:25, 1952.

Hyperkeratosis Ichthyosiformis Congenita

Association with Keratosis Areola Mammae Neviformis, Low-Grade Feeblemindedness, Bone Deformities, and Pseudopelade

DANILO STEVANOVIC, M.D., M.Sc. (Cantab), and SAVA KONSTANTINOVIC, M.D., Belgrade, Yugoslavia

The skin condition hyperkeratosis ichthyosiformis congenita (H. I. C.), in the greatest number of cases inherited as a recessive, has been also reported in a few instances as being associated with some other anomalies.

Review of Literature

The direct relationship between H. I. C. and oligophrenia was first suggested by Heinrichs.[1] This problem was later discussed by Bredmose[2] and recently fully investigated by Sjögren and Larsson.[3] In an extensive study from Sweden (with only three exceptions the parents of all patients were born in the county of Vasterbotten), they found a frequent association of oligophrenia and spastic disorders with H. I. C. Spastic disorders were mainly manifested as Little's disease. Eye changes manifested as degeneration of the pigment epithelium of the macula and its surroundings were diagnosed in the same group in three cases.

The association of some other psychological abnormalities, such as psychosis, idiocy, epilepsy, and dementia of the paranoid type, has been also reported.[1-7]

H. I. C., together with infantilism, genital atrophy, tetany, epilepsy, polyneuritis, and hyperchromic macrocytic anemia in one patient and with hypogenitalism, eunuchoidism, partial gigantism of the long bones, hyperglycemia of diabetic type in another patient, was reported by Rud.[8,9] Imbecility and hypogenitalism with H. I. C. were reported by Wiersema,[10] and infantilism and dementia with the latter, by Saethre.[11] On the other hand, presence of pubic hair in an 8-year-old girl with H. I. C., whose intellect was above normal, was reported by Gaté.[12] Disturbances in sexual development were also observed by Schwartz and colleagues.[13]

The association of osteoporosis,[14] acromegaly,[15] and disturbances in the sense of hearing [16] was also reported.

The abnormal laboratory findings found in some cases of H. I. C. were as follows: polycythemia, higher hemoglobin content, relative lymphocytosis, lower basal metabolic rate,[17] hyperchromic macrocytic anemia, and hyperglycemia.[8,9]

Report of a Case

The patient, aged 21, was born at term, with normal delivery. Skin changes were present at birth and bone deformities soon after. Redness of the skin was never pronounced, although it had been visible previously.

His parents were healthy. They were not blood relatives, but they both came from the same small village. There was no similar or other skin condition in the family.

On objective examination, the skin of the whole body, with the exception of trunk and face, was covered by thick or thin keratotic scales, particularly numerous on both lower extremities (Fig. 1). The skin of the affected parts was blackish; on the side of the neck and in the axillar folds black keratotic masses simulated acanthosis nigricans. The cubital and popliteal regions particularly were among the most involved.

Around the nipples black warty lesions, terminating sharply at the border of the areola mammae, were seen (Fig. 2).

On the scalp, mainly in the vertex region, there were small and large round and irregular patches where there was no hair. The skin of these areas was atrophic. Apart from this, the hair was of normal appearance. There was no excessive seborrhea (Fig. 3).

Submitted for publication Nov. 12, 1958.

From the Department of Dermatology and Venereology, University of Belgrade (Head, Prof. S. Ilic, M.D.).

The teeth were saw-like and not well cared for. Mucosa of the mouth and tongue was not affected.

On psychological examination, low-grade feeblemindedness was found. The intelligence corresponded to that of a 15-year-old person.

X-ray examination of the long bones showed severe deformities, with osteoporosis. The diagnosis of rickets was made.

Ophthalmological examination did not reveal any abnormality.

Figure 1

Laboratory findings: Red and white blood cell counts and hemoglobin concentration were within the limits of normal. All other laboratory investigations, including blood sugar, did not reveal any abnormality. Serological tests for syphilis were negative.

Comment

Skin changes in this case were typical.

Apart from low-grade feeblemindedness, several other points are of interest.

The association of keratosis areolae mammae neviformis with H. I. C. deserves

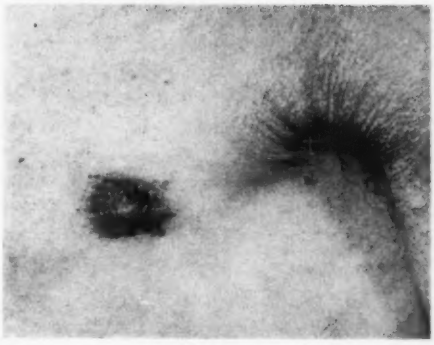


Figure 2

attention. The former condition is known in two forms: (1) symptomatic, usually as a sequela to eczema or any other inflammation of the areolae mammae, and (2) idiopathic, which is considered to be of nevoid origin, also called by Moncorps [18] "naevi keratodes."

Otto,[19] in 1929, speculated on keratosis areolae mammae neviformis as a possible abortive form of H. I. C. Our case substantiates this hypothesis.

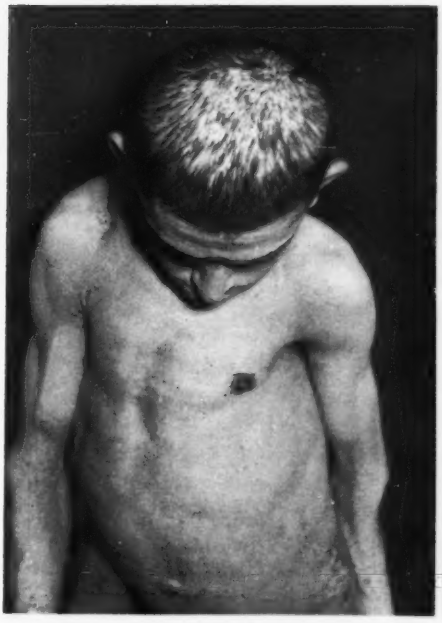


Figure 3

Bone deformities were mentioned by Liebermann.[20] There is, however, the question, as the author states, whether the case was one of H. I. C. since the redness of the skin appeared only when the patient was 10 years old.

Atrophic alopecia of the type "pseudopelade," of Brocq, though an acquired skin condition, is by its comparative rarity and its association with another rare condition, H. I. C., worthy of mention.

Summary

The literature on the association of hyperkeratosis ichthyosiformis congenita (H. I. C.) with some other anomalies is reviewed, and a new case is reported. The interesting features of this case are keratosis areolae mammae neviformis and pseudopelade of Borcq.

46a Nemanjina St.

REFERENCES

1. Heinrichs, J.: Norsk. mag. lægevidensk. 81: 1920; cited by Sjögren.[8]

2. Bredmose, G. V.: Nord. med. tidskr. 14:1453-1456, 1937; cited in Zentralbl. Haut- u. Geschlechtskr. 58:445, 1938.

3. Sjögren, T., and Larsson, T.: Acta psychiat. et neurol. scandinav., Vol. 32, Supp. 113, 1957.

4. van Bogaert, L.: Rev. neurol. 63:353-398, 1935.

5. Laubenthal, F.: Ztschr. ges. Neurol. u. psychiat. 163:233-238, 1938.

6. Stewart, R. M.: J. Ment. Sc. 85:256-263, 1939.

7. Ewing, J. A.: Am. J. Ment. Deficiency 60: 98-114, 1955.

8. Rud, E.: Hospitalstid. 70:525-538, 1927; cited by Sjögren.[8]

9. Rud, E.: Hospitalstid 72:426-433, 1929; cited by Sjögren.[8]

10. Wiersema, M. U.: Nederl. tijdschr. geneesk. 4764, 1937; cited in Zentralbl. Haut- u. Geschlechtskr. 58:273, 1938.

11. Saethre, H.: Norsk. mag. lægevidensk. 85: 126-134, 1924; cited in Zentralbl. Haut- u. Geschlechtskr. 13:449, 1924.

12. Gate, J., and Michel, P.: Bull. Soc. franç. dermat. et syph. 37:36, 1930.

13. Schwartz, L. L.; Bushman, G. J., and Woodburne, A. R.: Arch. Dermat. & Syph. 22:1106-1107, 1930; cited in Zentralbl. Haut- u. Geschlechtskr. 37:363, 1931.

14. MacGillivray, R. C.: Am. J. Ment. Deficiency 59:67-72, 1954.

15. Moeller, E.: Ugesk. læger 86:35, 1924; cited in Zentralbl. Haut- u. Geschlechtskr. 15:433, 1925.

16. Wintermitz, in Handbuch der Haut- und Geschlechtskrankheiten, edited by J. Jadassohn, Berlin, Springer-Verlag, 1931, Vol. 8.

17. Hüllstrung, H.: Zentralbl. Haut- u. Geschlechtskr. 54:487, 1937.

18. Moncorps, C., in Handbuch der Haut- und Geschlechtskrankheiten, edited by J. Jadassohn, Berlin, Springer-Verlag, 1931, Vol. 8.

19. Otto, K., cited by Moncorps.[18]

20. Liebermann, S.: Deutsche dermat. Wchnschr. 2:1881, 1931.

Familial White Folded Dysplasia of the Mucous Membranes

EDWARD V. ZEGARELLI, D.D.S.; FRANK G. EVERETT, D.M.D.; AUSTIN H. KUTSCHER, D.D.S.; JOHN GORMAN, M.D., and NORMAN KUPFERBERG, B.S., New York

In 1935, Cannon [1] first called attention to a syndrome which he described as a white spongy nevus of the oral mucosa. A detailed review of the medical and dental literature since that time has revealed 10 additional reports dealing with such a congenital disturbance of the oral mucous membranes. It has been variously termed "congenital leukokeratosis of the oral mucosa" by Ludy and Shirazy,[2] "pachyderma oralis" by Kinney and Derifield,[7] and "white folded gingivostomatosis" by Everett and Noyes,[5] Orban and Wentz,[6] and Darling and Fletcher.[12] Cooke [8,9] described two similar cases as "oral epithelial nevi." Lesions in the same patient in areas other than oral (dermal, vaginal, or rectal) have been documented in several of these reports.[5,11] A total of 15 cases have been actually observed and described in detail previously. Our review of the literature revealed that previously published reports contained relatively fragmentary and uncorrelated information with regard to the gross appearance and histopathological aspects of the syndrome. Therefore, we have made an attempt to gather together from the reporting investigators as much histopathologic material, clinical kodachrome photographs, and clinical history as was available, with the hope that intensive study of a larger body of material, all available for review at one time and by one group of investigators, might be rewarded with a more comprehensive understanding of this syndrome.

Accordingly, we wrote to the authors of each paper which had come to our attention, explaining our purpose and requesting their cooperation to the extent of providing us with any biopsy materials still available, any photographs of the lesions, as comprehensive a history as possible, and any additional data which had not been published in their original publication. We have thus come into the possession of material comprising cases representing five reports in the literature. We are herewith reporting also on eight additional patients, five of whom (Table 4) are relatives of two patients previously described [5] and three of whom (Table 5) have been seen by other investigators who have made their material available to us. In the remaining instances, the original material was no longer available.

Natural History

Some children have apparently been born with this abnormality. Others first show it in infancy or childhood or during adolescence. In most cases described in the literature and in those observed by us, this condition is of a relatively mild nature, reaching its full severity and extent in adolescence. On the basis of present clinical observations, it may be assumed that no further changes in the lesions occur during the rest of the person's life. It appears that there is a hereditary involvement.

Submitted for publication Nov. 9, 1958.

The following investigators assisted in this study: Drs. E. Shirazy, R. D. Kinney, R. S. Derifield, J. R. Trott, H. J. Noyes, H. E. Grupe, D. F. Mitchell, and B. Orban.

From the Division of Stomatology, School of Dental and Oral Surgery of the Faculty of Medicine, Columbia University, New York; the Department of Periodontology, University of Oregon Dental School, Portland, Ore., and the Institute of Cancer Research, Columbia University College of Physicians and Surgeons, New York.

TABLE 1.—*History, Physical Findings, and Distribution of Lesions Observed in Patients with White Folded Dysplasia of the Oral Mucous Membranes* *

Findings	Reference No. (Case)											
	7 (1)	2 (2)	11 (3)	11 (4)	11 (5)	5 (Rob.)	5 (Don.)	16 (Pat.)	16 (Bev.)	16 (David)	16 (Rich.)	16 (Daniel)
Age	42	27	31	6	10	32	35	7	5	8	7	4
Age first noted	Child	Birth	Infant			11	13	I		I	I	
Sex	M	F	F	M	M	M	M	F	F	M	M	M
Race		W				W	W	W	W	W	W	W
Present in												
Mother		*		*	*	II	II					
Father			*			II	II	*	*	*	*	*
Male child			*				*					
Female child						*						
Grandparents		1		1	1	II	II	II	II	II	II	II
Brothers (B) and/or sisters (S)		2S				B	B	S	S	B	B	B
Other relatives						See Table 4						
Previous history												
Normal		*	*			See Table 4						
Other	Myxedema asthma											
Distribution												
Skin		—										
Cheek, mucosa of	*	*	*	*	*	*	*	*	*	*	*	*
Gingivae		*	*				*					
Floor of mouth	*		*			*	*	*	*	*		
Ventral surface of tongue	*					*	*	*		*	*	
Dorsum of tongue	*		*			III	III				*	III
Sides of tongue	*		*			IV					*	
Fauces		*										
Hard palate	*	*										
Soft palate	*	*				*	*					
Inner lips		*	*			*	*	*	*			
Alveolar processes	*					*	*					
Vagina	—	—	*					II	II			
Rectum & anal canal	—	—						II	II			
Respiratory		—				V	V	II	II	V	V	
Urinary		—						II	II			
Gastrointestinal		—						II	II			

* I indicates no oral symptoms reported at the time of report *; II, according to reports of the patients; III, folded tongue; IV, crenated, and V, has respiratory symptoms (whether connected with the condition under discussion, we do not know).

TABLE 2.—*Symptomatology, History, and Clinical Findings in Patients with Familial White Folded Dysplasia of the Mucous Membranes* *

Objective & Subjective Symptomatology	Reference											
	7	2	11	11	11	5	5	16	16	16	16	16
None	•			•	•							
Burning						I	I					
Pain or soreness						I	I					
Soft			•	•	•	•	•	•	•	•	•	•
Spongy						•	•	•	•		•	•
Thickened mucosa	•			•	•	•	•	•	•		•	•
Pearly	•		•	•	•							
White	•	•	•	•	•	•	•			II	•	•
Folded			•	•	•	•	•	•	•	•	•	•
Furrowed with crypts	•											
Milky film		•						•	•	•		
Loose, supple, flexible		•	•	•	•							
Villous		•										
Scrapes off without bleeding		•										
Cracking of corners of mouth			•									
Malignancy		—	—	—	—							
Vesiculation						•	•					•
Desquamation						•	•			•		•

* I, indicates consumption of acid and highly seasoned food only, and II, in isolated spots on the cheek primarily.

Clinical Observations

A summary of the facts surrounding this syndrome as observed in our studies suggests a clinical picture of an unusually rare familial disease in which some portions or even all of the oral mucous membranes may have a deeply folded or corrugated-like character with a soft, keratotic-like surface (Figs. 1 and 2).

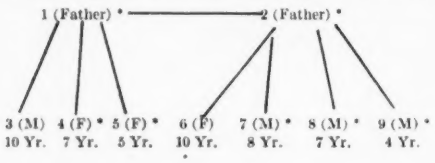
In some instances, a similar involvement of other mucous membrane surfaces of the body has been observed. Two such cases

TABLE 3.—*Histopathology Evidenced by Biopsy Specimens in Eight Patients Studied*

	Reference *						
	2†	10	7	5	5	5	11
Epithelium							
Parakeratosis			1+				
Keratosis		4+	1+	1+	1+	1+	1+
Thickening of epithelium	4+	1+	3+	4+	4+	4+	4+
Hyperplasia of basal-cell layer	1+	—	1+	2+	2+	1+	2+
Rete pegs irregular in size							
Prominent rete pegs		2+	—	—	1+	1+	2+
Intraepithelial vesicles							
Vacuolation of cells		—	1+	4+	4+	2+	4+
Glycogen in cells							+
Acanthosis	3+	0	3+	4+	4+	3+	4+
Corium							
Scarring of hyaline degeneration		3+	—		1+	—	—
Keratohyaline granules		1+	1		1+	2+	?
Edema		—	—	—	—	—	—
Hydropic degeneration				1+	1+		
Nonspecific inflammation		3+	+		4+	—	—
Polymorphonuclear leukocytes							
Lymphocytic infiltration		2+	1+		1+		
Vascular stroma		2+	1+		1+	1+	1+
Perivascular infiltration		2+	—	—	—	—	—
Tissue spaces & exudate		—	—	—	—	—	—
Separation of layers		—	—	—	—	—	—
Mast cells		6+	1+	—	—	1+	—
No nuclei		—	1+	1+	1+	1+	—
Pyknotic nuclei		—	1+	—	—	—	—
Increased mitotic figures basal layer		—	2+	—	+	1+	4+

* The numbers before the plus signs signify the frequency or severity of the disturbance.
† Photomicrograph of original section does not reveal cellular detail.

TABLE 4.—*Family Tree*



Case No.	Findings	Oral Lesions
1	Proctoscopic negative; thickening of the tympanic membrane; transitional first sacral vertebra	Present
2	Proctoscopically negative; no other significant findings either	Present
3 †		Not present
4 †		Present
5 †		Present
6	Minimal hemorrhoids, ear infection, ozena, respiratory trouble	Not present
7	Ozena, respiratory trouble; proctoscopically negative	Present
8	Rose fever, asthma (allergies); proctoscopically negative; enamel hypoplasia	Present
9	Colitis early in life; not now; proctoscopically negative	Present

* Has the oral lesions.

† No known skin lesions nor changes in the (nonoral) mucous membranes. No proctoscopic nor genital findings available.

have been reported. Vaginal biopsy specimen from one of these revealed findings essentially similar to those noted for the oral mucous membranes (see below).

Further details of each case previously described in the literature may be found in the originally reported studies. Pertinent details (all those available) are presented on three additional patients with familial white folded dysplasia of the mucous membranes, in all of whom intraoral examinations revealed findings typical of those described for this disease.

TABLE 5.—*Pertinent Details, All Those Available, on Three Additional Patients with Familial White Folded Dysplasia of the Mucous Membranes on All of Whom Intraoral Photographs Revealed Findings Typical of Those Described for This Disease*

Case No.	Findings
1	No other members of family afflicted; biopsied 4 yr. ago but no diagnosis made; condition has not changed since discovered; tender & slightly painful at times; no other ectodermal dysplasia; negative serology; normal proctoscopic examination[14]
2	28-yr.-old housewife; referred by family dentist because of unusual sloughing of oral mucosa of both cheeks; disseminated over cheeks & lips; first noticed 5 yr. previously; has unsuccessfully attempted to control lesion by elimination diet; 3 dermatologists suggested metallic reaction associated with galvanism; does not smoke; has been careful with dentifrice; complete physical check-up not revealing; brother & sister have had similar condition, according to patient, for "several years"; since observation began, patient has continued to be in good health[14]
3	Soldier, about 18-20 yr. of age; shed mucous membrane (at least hyperkeratotic surface) every once in a while[13]

The salient features (where available) of the histories of the patients whose biopsy specimens were studied in our laboratories have been summarized in Table 1.

The characteristics (clinical) of the oral lesions of the patients under consideration herein appear in Table 2.

Histopathologic Observations

The histopathologic findings seen in the biopsy specimens studied in our laboratories have been summarized in Table 3.

Fig. 1.—Clinical appearance of oral mucosa in 7-year-old girl (not previously reported) with familial white folded dysplasia, reported by Everett.[16]

Fig. 2.—Clinical appearance of oral mucosa in 27-year-old man (not previously reported) with familial white folded dysplasia, reported by Grupe.[15]

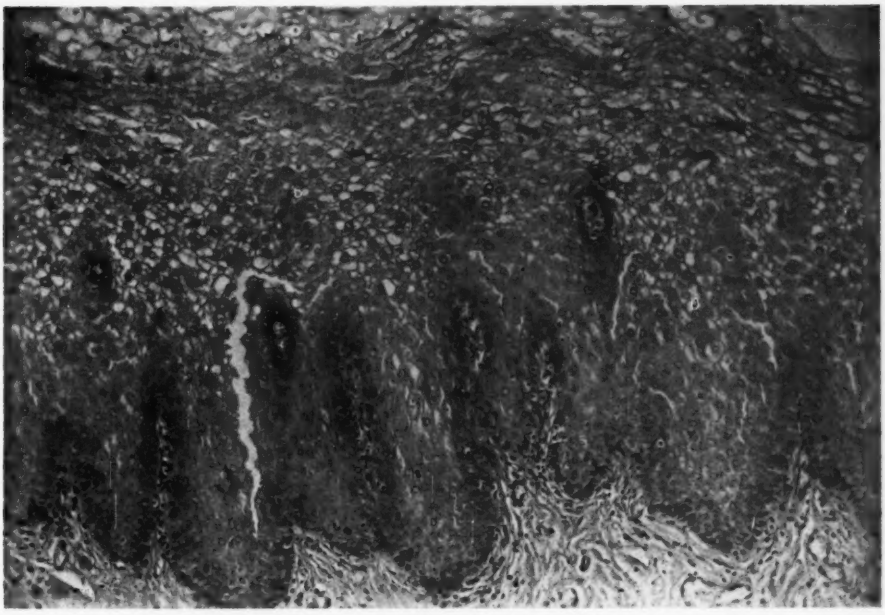
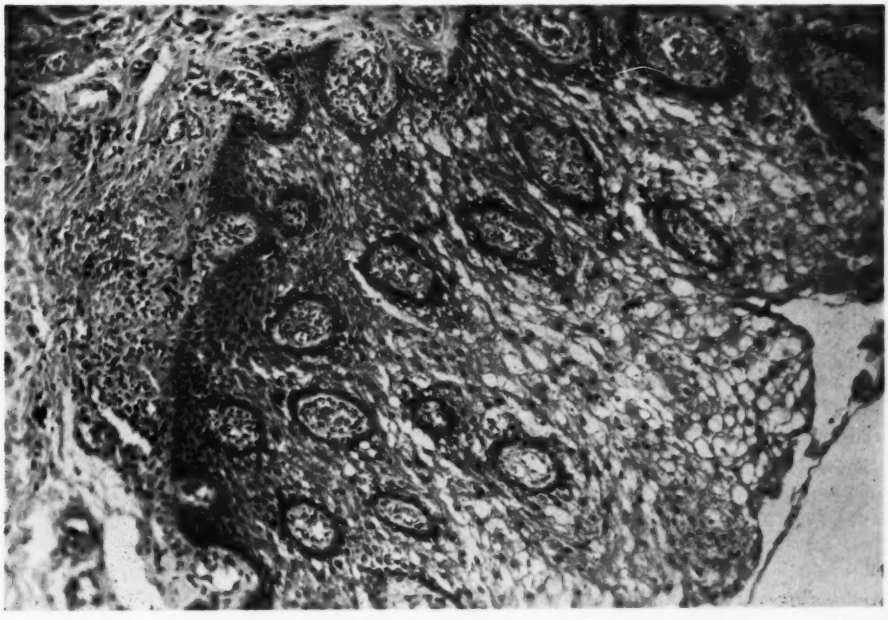


Fig. 3.—Typical histopathology seen in oral mucosa in 27-year-old man (not previously reported) with familial white folded dysplasia, reported by Grupe.[15]

Fig. 4.—Typical histopathology seen in oral mucosa in 28-year-old woman (not previously reported) with familial white folded dysplasia, reported by Mitchell.[14]



Our investigation resulted in the following pertinent findings: Histologically (Figs. 3 and 4), a typical biopsy specimen of involved mucous membrane shows a marked thickening of the epithelium. This is due to a hyperplasia and/or vacuolation of all layers. Normal stratification of layers is visible in most instances. Occasionally the observation of this finding is somewhat difficult. All epithelial cells show normal polarity. No bizarre nuclei are in evidence, although nuclei were pyknotic in one section.

Parakeratosis is a frequent finding, the epithelium being up to 45-50 cells thick.

There was marked acanthosis with *many* mitoses in two additional sections. Many cells show *marked swelling and vacuolation* (containing glycogen in at least one of the biopsy specimens studied) in the granular and prickle-cell layer. Occasionally, keratohyaline granules are seen in the granular and prickle-cell layers. The basal layer of cells is markedly hyperplastic, with irregular rete pegs projecting into the corium.

In the *corium*, inflammation is not a characteristic finding, although a nonspecific inflammatory process was observed in three specimens. Marked vascularity of the stroma is seen in all sections. Edema is not conspicuous.

The specimen of tissue from the vagina of one patient previously reported [11] revealed characteristics essentially similar to those seen in the oral tissue but with a more orderly arrangement of the thick layer of squamous epithelial cells. In addition, the vaginal tissue differed from the cheek tissue in that it lacked keratin. The only changes evidenced in both cheek and vaginal sections were observed in the surface epithelium. In both tissues the lamina propria was normally vascular and its stroma showed no thickening of fibers. There was no inflammation of consequence in either tissue. Since considerable vacuolation was noted in both the vaginal and the oral histologic preparations studied on this patient, a second biopsy specimen was taken from the mucosa of the right cheek in the area of the lower molar teeth. The tissue was obtained from an area in which Fordyce's spots were clinically evident but which was free of trauma and cheek-biting. Periodic acid-Schiff (PAS) glycogen determinations were performed in addition to routine sections stained with hematoxylin and eosin. Findings in the sections stained with hematoxylin and eosin were similar to those previously noted in the earlier biopsy specimen and included a thickened, well-differentiated, moderately keratinizing, stratified squamous epithelium without loss of polarity or orderliness of stratification. PAS glycogen stain revealed purplish-red glycogen-positive granules in the cytoplasm of many of the epithelial cells. The proof of their being glycogen was substantiated by their absence in the PAS control, owing to the action of the enzyme diastase from saliva.

Our review of the slides suggested that the patients described by Trott [10] do not fall into the same disease classification as do our patients. Although the clinical picture in Trott's patient in a localized area was reminiscent of the lesion under consideration, it was confined to a small area of the gingivae clinically. Microscopically, there was a marked difference. The keratosis was much more pronounced; the total thickness of the epithelium was much less. Basal-cell hyperplasia, acanthosis, mitotic figures, and vacuolation of the cells were absent. Considerably more scarring or hyaline degeneration, nonspecific inflammation, and a more vascular stroma with perivascular infiltration were seen in the corium. Mast cells were noted. The picture was rather that of hyperkeratosis. For the above reasons we hesitate to consider the material published by Trott as representative of a case of familial white folded dysplasia of the oral mucous membranes.

Summary

Increasing attention has been devoted recently to a peculiar congenital disturbance of the oral mucous membranes, characterized by a white folded dysplasia coupled with diffuse dyskeratosis of the oral mucous membranes, giving them a deeply folded or

corrugated appearance with a dense grayish white keratotic surface. Pertinent data dealing with a total of 16 patients, including 8 subjects who had been described in reports appearing in the literature and 8 persons reported on for the first time, have been gathered together and are herewith presented.

Our observations of histopathologic material suggest that the epithelial changes are caused by the usual normally ordered thickening of all layers of the mucous membrane. Parakeratosis is a frequent finding, the epithelium being up to 45-50 cells thick. There was marked acanthosis with *many* mitoses in the basal and prickle-cell layers in one biopsy specimen and somewhat fewer mitoses in two additional sections. Many cells show marked swelling and vacuolation (containing glycogen in at least one of the biopsies studied) in the granular and prickle-cell layers. The epithelial cells and their arrangement have an entirely benign appearance.

630 W. 168th St. (32) (Dr. Kutscher).

REFERENCES

1. Cannon, A. B.: White Nevus of the Mucosa (Naevus Spongiosus Albus Mucosae), Arch. Dermat. & Syph. 31:365, 1935.

2. Ludy, J. B., and Shirazy, E.: Congenital Leukokeratosis Mucosa Oris, Internat. Clin. 4:38, 1941.

3. Lynch, F. W.: Leukokeratosis Oris, A. M. A. Arch. Dermat. & Syph. 63:145, 1951.

4. Gandy, D. T.: Nevus Spongiosus Albus Mucosae: Report of Case, Texas J. Med. 48:145, 1952.

5. Everett, F. G., and Noyes, H. J.: White Folded Gingivo-Stomatosis, J. Periodont. 24:32, 1953.

6. Orban, B. J., et al.: Atlas of Clinical Pathology of the Oral Mucous Membrane, St. Louis, The C. V. Mosby Company, 1955, p. 94.

7. Kinney, R. C., and Derifield, R. S.: Pachyderma Oralis: Report of Case, J. Oral Surg. 14: 71, 1956.

8. Cooke, B. E. D.: Oral Epithelial Nevi, J. Dent. Res. 35:954, 1956.

9. Cooke, B. E. D.: Leucoplakia Buccalis and Oral Epithelial Naevi: A Clinical and Histological Study, Brit. J. Dermat. 68:151, 1956.

10. Trott, J. R.: Congenital Keratosis of the Gingiva, Dental Practitioner 6:348, 1956.

11. Zegarelli, E. V., and Kutscher, A. H.: Familial White Folded Hypertrophy of the Mucous Membranes: Report of 3 Cases, Oral Surg. 10: 262, 1957.

12. Darling, A. I., and Fletcher, J. P.: Familial White Folded Gingivostomatosis, Oral Surg. 11: 296, 1958.

13. Orban, B.: Personal communication to the the authors.

14. Mitchell, D. F.: Personal communication to the authors.

15. Grupe, H. E.: Personal communication to the authors.

16. Everett, F. G.: Unpublished data.

Histopathology of Pemphigus Foliaceus

TANCREDO A. FURTADO, M.D., Belo Horizonte, Brazil

Since the outstanding work of French and Belgian dermatologists, many papers have appeared in the literature stressing the value of the histopathologic picture in the diagnosis of the diseases of the pemphigus group. A review of the subject shows that a consensus among authorities has not yet been reached. Most studies refer to pemphigus vulgaris and its differentiation from dermatitis herpetiformis of Duhring-Brocq. In Brazil pemphigus vulgaris, pemphigus vegetans, pemphigus of the mucous membranes, and familial benign chronic pemphigus are exceptionally rare entities, whereas pemphigus foliaceus and pemphigus erythematosus (which we consider a forme fruste of pemphigus foliaceus) are very frequent. In this paper I am presenting detailed histopathological study of pemphigus foliaceus.

Submitted for publication Sept. 4, 1958.

This is an abridgment of a paper presented before the XV Annual Meeting of the Brazilian Dermatological Society, July 7-10, 1958.

Associate Professor in charge of the Histopathology Section, Dermatologic Clinic, Faculty of Medicine, University of Minas Gerais (Chairman: Prof. Olyntho Orsini), from the National Institute of Rural Endemic Diseases (Director: Prof. Amilcar Vianna Martins).

Review of Literature

The problem of histopathological differentiation of bullous diseases has been focused on pemphigus, dermatitis herpetiformis, and erythema multiforme. In the classical textbooks of skin pathology [1-4] it is stated that there is no diagnostic histologic appearance for each of these entities. In 1936, Civatte [5] was the first to call attention to the phenomenon of acantholysis, (a loss of coherence between epidermal cells due to degeneration of the intercellular bridges) as a microscopic change characteristic of pemphigus. Afterward many other publications, from different countries, appeared in the literature. In a review of the subject we may separate two currents of opinion: (1) those who state that the intraepidermal acantholytic bulla is a constant feature of pemphigus and the subepidermal tension type of bulla is only seen in

TABLE 1.—*Authors with First Opinion* *

Author	Yr.	Country	Cases Studied, No.				
			P. Fol.	P. Erit.	P. Veg.	P. V.	D. H.
Dupont & Pierard [6,7]	1938 & 1949	Belgium	?	?	?	?	?
Laplère et al. [8]	1946 & 1949	Belgium	?	?	?	?	?
Orsini [9]	1946	Brazil	3	—	—	—	—
Kuhn & Iverson [10]	1948	United States	—	—	—	4	—
Rabelo et al. [11]	1949	Brazil	?	?	?	?	?
Rook & Whimster [12]	1950	England	—	—	—	1	2
Lever [13]	1951	United States	13	1	4	41	—
Szodoray et al. [14]	1951	Hungary	—	1	—	6	2
Nazzaro [15]	1952	Italy	—	—	—	14	6
Director [16]	1952	United States	—	—	—	33	—
Wentholt & Jansen [17]	1952	Holland	—	—	—	2	—
Rook & Wadington [18]	1953	England	—	—	—	16	—
Brennan [19]	1953	United States	1	—	1	13	—

* Authors who believe that (1) acantholysis and intraepidermal bulla are present in true pemphigus, and (2) no acantholysis and subepidermal bulla are present in dermatitis herpetiformis.

TABLE 2.—*Authors with Second Opinion* *

Author	Yr.	Country	Cases Studied, No.					Observations
			P. Fol.	P. Erit.	P. Veg.	P. V.	D. H.	
Civatte[20,21]	1943 & 1949	France	1 ?	 ?	1 ?	1 ?	7 ?	Acantholysis & intraepidermal bulla in true pemphigus; subepidermal & subcorneal bulla in D. H.
MacCardle et al.[22]	1943	United States	—	—	—	8	—	Absence of acantholysis, subepidermal bulla or intraepidermal bulla continuing with subepidermal bulla in P. V.
Allen[23]	1948	United States	2	3	2	4	50	—
Alayon[24]	1948	Brazil	20	—	—	—	1	Acantholysis & intraepidermal bulla in P. Fol.; rarely subepidermal bulla in P. Fol.; subepidermal bulla & rarely intraepidermal bulla in D. H.
Fassotte[25]	1948	Belgium	—	—	—	2	2	No acantholysis & subepidermal bulla in P. V.; acantholysis & intraepidermal bulla in D. H.
Portugal[26]	1949	Brazil	5	2	2	1	5	Acantholysis in true pemphigus; subepidermal, intraepidermal & subcorneal bulla in D. H.
Percival & Hannay[27]	1949	England	—	1	—	5	6	Subepidermal bulla in P. V. & D. H.; subgranular & subcorneal bulla in P. Erit.
Nelemans[28]	1951	Holland	3	—	—	4	5	Subepidermal bulla & no acantholysis in one case of P. V.
Winer & Lipschultz[29]	1952	United States	—	—	—	9	3	Acantholysis in true pemphigus; intraepidermal & subepidermal bulla in P. V.
Nieuwmeijer[30]	1953	Holland	1	1	—	2	8	Intraepidermal acantholytic bulla in true pemphigus & subepidermal tension bulla in D. H.; subepidermal bulla & acantholysis in 2 cases of D. H.
Brennan & Montgomery[31]	1953	United States	14	5	17	45	—	Acantholysis: 85% in P. Fol., 100% in P. Erit., 52% in P. Veg., & 53% in P. V.
Hellier[32]	1954	England	—	—	—	1	—	Subepidermal bulla & no acantholysis in P. V.
Ziberberg[33]	1955	Brazil	7	8	7	10	13	Intraepidermal acantholytic bulla in true pemphigus; subepidermal, partially subepidermal, & intraepidermal bulla in D. H.
Steigleder[34]	1955	Germany	—	—	—	20	—	Acantholysis in P. V., in virus bullae diseases, in pustular psoriasis, in banal pustule, & in cantharidin blister; intraepidermal & subepidermal bulla in P. V.
Fisher[35]	1956	United States	—	—	—	52	—	Intraepidermal acantholytic bulla in P. V. (30.7%); subepidermal tension type bulla in P. V. (69.3%)

* Thoses who believe location of bulla and/or acantholysis are variable and inconstant in various forms of pemphigus and dermatitis herpetiformis.

dermatitis herpetiformis (Table 1); (2) those who think that the site of the bulla and acantholysis are not uniform and invariable in each disease (Table 2). In this review I omit erythema multiforme, which I believe can be diagnosed on clinical grounds by its symptomatology and evolution. The work of many authors [25,30,31,35,38] shows that the presence of acantholysis does not mean a bad prognosis; neither is its absence a sign of good prognosis, as Dupont and Pierard [6] and Civatte [5] had assumed.

Material and Method of Study

A study was made of 213 sections from 183 patients having a clinical diagnosis of pemphigus foliaceus. I examined only one section from most patients, for biopsies were done as a routine diagnostic procedure. The last 17 sections were from patients still hospitalized. For the rest of the material a careful review of each section was made on the basis of the new ideas in the matter. The clinical diagnosis was always made by competent dermatologists. All sections were stained by hematoxylin and eosin, and a small number by Van Gieson's and Gomori's method also, for the study of intercellular fibrils.

Results and Comment

The commonest and most characteristic feature found was acantholysis in the upper portion of the epidermis, leading to the formation of a cleft, which may be either subcorneal, just below the granular layer, in the upper part, or, rarely, in the middle of the rete Malpighii (Fig. 1*A*). As the cleft increases in size it may cause the detachment of the upper part of epidermis, without bulla formation (Fig. 1*B*), a frequent event, or it may develop into an intraepidermal bulla, usually superficial. Depending on the site of the level of cleavage, the roof of the bulla or of the detached epidermis may be composed of the horny layer alone, of the horny and granular layers, or of the horny and granular layers together with one to several rows of Malpighian cells. Sometimes the three situations are represented in one single bulla (Fig. 1*C*). The floor is formed in each case by the rest of the epidermis below. Inside a tense or ruptured bulla, usually near its limits, acantholytic cells may be seen in varied numbers but always showing a characteristic appearance, including absence of intercellular bridges, homogenization of the cytoplasm, hyperchromasia of the nucleus, and a tendency to acquire a round shape (Fig. 1*D*). An intact bulla either may be flaccid, forming acute angles at its lateral edges, or it may be tense with rounded borders. The bulla may be empty or may contain a variable number of polymorphonuclear neutrophils, usually with a smaller number of eosinophils, and also usually accompanied by fibrin. In some instances it may change to a real pustule, in which case the Malpighian cells at the borders show reticular degeneration.

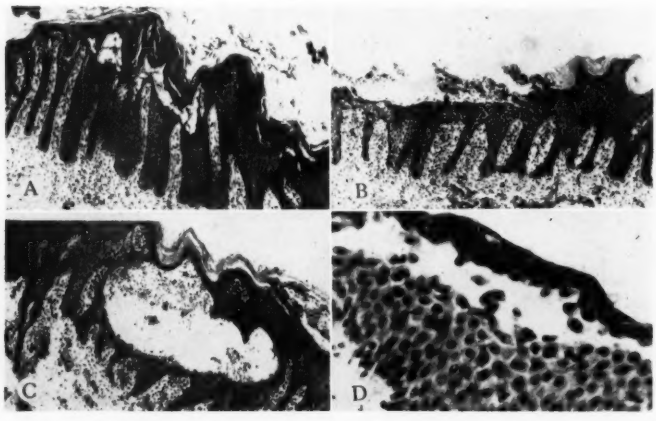


Fig. 1.—*A*, an early change in pemphigus foliaceus; subgranular cleft leading to the formation of a superficial intraepidermic bulla. Reduced 40% from mag. × 100. *B*, detachment of upper epidermis without bulla formation. Reduced 40% from mag. × 100. *C*, a tense bulla with rounded borders; acantholytic cells are seen near the floor; the roof is partly formed by horny and granular layers and partly by many rows of Malpighian cells. Reduced 40% from mag. × 100. *D*, free acantholytic cells inside a bulla. Reduced 40% from mag. × 450.

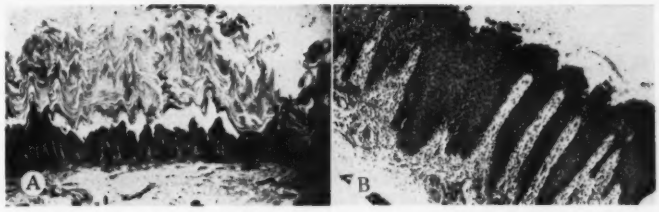


Fig. 2.—*A*, intense hyperkeratosis, acanthosis, and papillomatosis giving a frankly verruciform appearance; subcorneal cleavage is also seen. Reduced 40% from mag. × 25. *B*, psoriasiform aspect with acantholysis in the uppermost epidermis. Reduced 40% from mag. × 100.

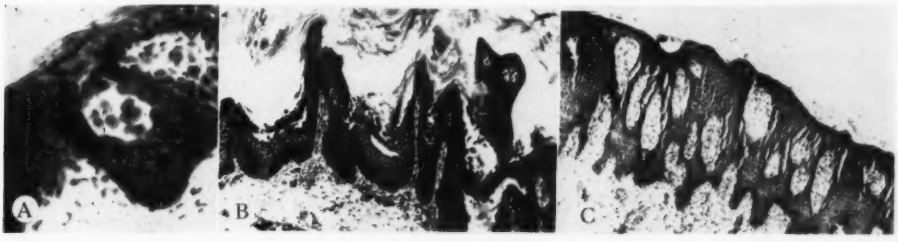
The changes just described are found in early cases of pemphigus foliaceus or when the newly formed lesions of chronic, long-standing cases are selected for biopsy. However, usually older lesions are sectioned for microscopic examination, and these show a somewhat different picture. The changes characteristic of chronic inflammation are seen; acanthosis is constantly found together with a varied degree of papillomatosis, hyperkeratosis, and follicular plugging with or without parakeratosis.* In a few cases the histologic picture resembled psoriasis or exfoliative dermatitis, but the presence of acantholysis in the uppermost portion of the epidermis disclosed the true diagnosis (Fig. 2*B*). Besides those changes other features were regularly observed which are consequent to acantholysis, such as segregation and dyskeratosis. By segregation I mean the separation of cells in the granular and Malpighian layers, individually or in groups, due to loss of intercellular bridges (Fig. 3*A*). The individual Malpighian cells show the degenerative changes already described for the acantholytic cells. The granular cells exhibit features similar to the corps ronds and grains of Darier's disease (Fig. 3*B*). Clefts in various levels of the epidermis, forming oblique or broken lines, were commonly observed (Fig. 3*C*), sometimes imitating the lacunae of keratosis follicularis (Fig. 3*B*). Increased pigment formation is another feature of chronic lesions, not only in the melanocytes of the basal layer but also in dermal melanophores. The pilosebaceous follicle may show all the changes found in the older lesions. The picture described is, in the absence of bullae, highly diagnostic of pemphigus foliaceus.

On the contrary, the dermis does not show significant changes. The capillaries in the papillae and upper corium are dilated, and there is a variable degree of edema. The inflammatory infiltrate may be diffuse or assume a perivascular and periadnexial distribution. It is composed of neutrophils, eosinophils, and lymphocytes, which are variably represented by usually small or moderate number.

The large number of sections available for study led me to make a statistical evaluation of the different changes, which were found

* Sometimes the appearance is frankly verruciform (Fig. 2*A*).

Fig. 3.—*A*, segregation: separation of epidermal cells in groups, due to acantholysis. Reduced 35% from mag. × 450. *B*, horizontal clefts and dyskeratotic changes of the granular cells, which resemble grains and corps rond of Darier's disease. Reduced 35% from mag. × 100. *C*, longitudinal clefts due to acantholysis. Reduced 35% from mag. × 100.



in the following percentages: subcorneal cleavage 29.4%, subgranular cleavage 38.2%, cleavage from middle epidermis up 53.9%, acantholytic cells 68.5%, bulla 47.1%, segregation 49.3%, dyskeratosis 38.5%, hyperkeratosis 31.9%, parakeratosis 18.4%, acanthosis 74.8%, papillomatosis 26.3%, pigmentation 24.5%, epidermal appendages changes 31.9%. The constancy of the phenomenon of acantholysis, with its resultant alterations (clefts, bullae, free acantholytic cells, segregation, and benign dyskeratosis) and their site in the epidermis, made a histopathological diagnosis possible in 91.8% of all cases with a clinical diagnosis of pemphigus foliaceus.

In the recent material from patients examined clinically acantholysis and/or dyskeratosis was found in 100%. It should be remembered that Brennan and Montgomery[31] observed acantholysis in only 52% of pemphigus vegetans and 53% of pemphigus vulgaris, while the figures for pemphigus foliaceus and pemphigus erythematosus was 85% and 100%, respectively.

Besides true pemphigus, acantholysis may also occur in familial benign chronic pemphigus, Darier's disease, viral bullae, senile keratosis, and in adenoacanthoma of sweat glands (Lever,[36] Graham and Helwig[37]). Recently, Steigleder,[34] through histopathological and cytologic studies, showed that so-called "pemphigus cells" could be found in psoriasis pustulosa, in banal pustules, and also in cantharidin blisters of normal persons. It should be pointed out, however, that for the latter conditions their microscopic changes and the clinical symptoms and signs pertinent to each one make the differential diagnosis an easy matter.

Summary

A review of the literature shows that there is no consensus regarding the value of histopathology in the diagnosis of pemphigus in all its forms.

This report concerns pemphigus foliaceus and consists of the microscopic examination of 213 sections taken from 183 patients.

Acantholysis is the basic and most constant histologic change in pemphigus foliaceus.

Acantholysis is responsible for the formation of cleavage, clefts, intraepidermal bullae, and the phenomenon of segregation of Malpighian and granular cells.

Clefts, segregation, and dyskeratosis (grains and corps ronds) are common features of chronic cases.

The older lesions show also in variable degree acanthosis, papillomatosis, hyperkeratosis, parakeratosis, and increased pigment formation.

All of the changes described are freguently seen involving the pilosebaceous follicle.

In any phase of the disease, the epidermal changes found and their location made the diagnosis of pemphigus foliaceus possible in 91.8% of all cases.

Prof. Oswaldo Costa, Dr. Moacyr Junqueira, and Prof. L. Bogliolo gave permission for use of their material in this study. Dr. Hugo Brandão helped in the preparation of the photomicrographs.

Rua Tupinambas, 360.

REFERENCES

1. Gans, O.: Histologie der Hautkrankheiten, Berlin, Springer-Verlag, 1925, Vol. 1, p. 251.

2. Riecke, E.: Pemphigus, in Jadassohn, J.: Handbuch der Haut und Geschlechtskrankheinten, Berlin, Springer-Verlag, 1931, Vol. 7, Pt. 2, p. 466.

3. MacLeod, J. M. H., and Meunde, L.: Practical Handbook of the Pathology of the Skin, New York, Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 1946, p. 91.

4. McCarthy, L.: Histopathology of Skin Diseases, St. Louis, The C. V. Mosby Company, 1931, p. 153.

5. Civatte, A.: Histopathologie génerale, in Darier, J. et al.: Nouvelle pratique dermatologique, Paris, Masson & Cie, 1936, Vol. 1, p. 311.

6. Dupont, A., and Piérard, J.: Dermatoses bulleuses in Traité de dermatologie clinique et thérapeutique, Paris, Gaston Doin & Cie, 1938, Vol. 2, Fascicle 1, pp. 494, 515.

7. Dupont, A., and Piérard, J.: Histologie du pemphigus chronique et de la dermatite de Duhring-Brocq, VIIème Congrès des Dermatologistes et Syphiligraphes de Langue Française, Bruxelles-Liège, 21 au 23 avril 1949, Imprimèrie Lielens, Rapports, p. 97.

8. Lapière, S.; van Runckelen, H., and Dussart, L.: Valeur des critères histologiques pour le diag-

nostic entre pemphigus et dermatites polymorphes de Duhring-Brocq, Arch. belges dermat. et syph. 2:81, 1946.

9. Orsini, O. de C.: Aspectos epidemiológicos e clínicos do pênfigo foliáceo em Minas Gerais, Tese, Belo Horizonte, Imprensa Oficial, 1945, p. 147.

10. Kuhn, B. H., and Iverson, L.: Pemphigus Vulgaris: A Clinicoanatomic Study, Arch. Dermat. & Syph. 57:891, 1948.

11. Rabello, F. E.; Portugal, H., and Azulay, R. D.: Observations cliniques et recherches histologiques et biologiques dans les bulloses du groupe du pemphigus, VIIme Congrès des Dermatologistes et Syphiligraphes de Langue Française, Bruxelles-Liège, 21-23 avril, 1949, Communications et Discussions, Imprimèrie Lielens, p. 50.

12. Rook, A. J., and Whimster, I. W.: The Histological Diagnosis of Pemphigus, Brit. J. Dermat. 62:443, 1950.

13. Lever, W. F.: Pemphigus: A Histopathologic Study, A. M. A. Arch. Dermat. & Syph. 64:727, 1951.

14. Szodoray, L.; Vertes, F.; Racz, S., and Horvath, G.: Über einige aktuelle Fragen der Pathogenese des Pemphigus, Dermatologica 102: 125, 1951.

15. Nazzaro, P.: Lo studio citologico nele dermatosi bollose e vescicolari; raffronti comparativi con l'istologia, Minerva dermat. 27:280, 1952.

16. Director, W.: Pemphigus Vulgaris: A Clinicopathologic Study, A. M. A. Arch. Dermat. & Syph. 65:155, 1952.

17. Wentholt, H. M. M., and Jansen, E.: Some Observations on Pemphigus Vegetans, Dermatologica 105:100, 1952.

18. Rook, A., and Waddington, E.: Pemphigus and Pemphigoid, Brit. J. Dermat. 65:425, 1953.

19. Brennan, J. G.: Contributions to the Study of Pemphigus, A. M. A. Arch. Dermat. & Syph. 68:481, 1953.

20. Civatte, A.: Diagnostic histopathologique de la dermatite polymorphe douloureuse ou maladie de Duhring-Brocq, Ann. dermat. et syph. 3:1, 1943.

21. Civatte, A.: Le Diagnostic des dermatites bulleuses au laboratoire, VIIme Congrès des Dermatologistes et Syphiligraphes de Langue Française, Bruxelles-Liège, 21-23 avril, 1949, Rapports, Imprimèrie Lielens, p. 63.

22. MacCardle, R. C.; Baumberger, J. P., and Herold, W. C.: Histochemistry of Pemphigus Lesions, Arch. Dermat. & Syph. 47:517, 1943.

23. Allen, A. C.: Survey of Pathologic Studies of Cutaneous Diseases During World War II, Arch. Dermat. & Syph. 57:19, 1948.

24. Alayon, F. L.: Contribuição para o Estudo do Pênfigo Foliáceo (Fogo Selvagem) no Brasil, Rev. med. e cir. São Paulo 8:1, 1948.

25. Fassote, M.: Nouvelles observations cliniques, histologiques et biologiques dans les cas des dermatoses bulleuses du type pemphigus, Arch. belges dermat. et syph. 4:3, 1948.

26. Portugal, H.: Contribuição da histopatologia nas dermatoses do grupo do pênfigo, An. brasil dermat. e sif. 24:29, 1949.

27. Percival, G. H., and Hannay, P. W.: Observations on the Structure and Formation of Bullae, Brit. J. Dermat. 61:41, 1949.

28. Nelemans, T. G.: Pemphigus Vulgaris and Dermatitis Herpetiformis Duhring, Van Gorcum & Co. Assen., 1951.

29. Winer, L. H., and Lipschultz, C. E.: Comparative Study of Histology and Cytology in Vesiculating Eruptions, A. M. A. Arch. Dermat. & Syph. 65:270, 1952.

30. Nieuwmeijer, A. H.: Tonofibrils in Bullous Dermatoses: A Histo- and Cytopathologic Study, Dermatologica 106:379, 1953.

31. Brennan, J. G., and Montgomery, H.: Pemphigus and Other Bullous Dermatoses: Correlation of Clinical and Pathologic Findings, J. Invest. Dermat. 21:349, 1953.

32. Hellier, F. F.: Anomalous Histological Findings in Pemphigus, Brit. J. Dermat. 66:49, 1954.

33. Zilberberg, B.: Pênfigo e dermatite de Duhring-Brocq. Contribuição para o estudo histocitológico, Arq. dermat. e sif. São Paulo 16:43, 1955.

34. Steigleder, G. K.: Zur Differentialdiagnose des Pemphigus vulgaris aus dem Blasengrundausstrich, Arch. klin. u. exper. Dermat. 202:1, 1955.

35. Fisher, I.: Pemphigus Vulgaris: A Correlation of Clinical and Microscopic Observations, A. M. A. Arch. Dermat. 74:50, 1956.

36. Lever, W. F.: Histopathology of the Skin, Second Edition, Philadelphia, J. B. Lippincott Company, 1954.

37. Graham, J. H., and Helwig, E. B.: Isolated Dyskeratosis Follicularis, A. M. A. Arch. Dermat. 77:377, 1958.

38. Watrin, J., and Jeandidier, P.: Sur douze cas de maladie de Dühring, Ann. dermat. et syph. 78:551, 1951.

Subcorneal Pustular Dermatosis

ROBERT E. BURNS, M.D., and GERALD FINE, M.D., Detroit

Knowledge of the bullous dermatoses has advanced with the more liberal application of the biopsy, allowing not only a more definitive classification of these eruptions but also an introduction of new members to the group. A newcomer among the vesicular and bullous diseases of the skin is subcorneal pustular dermatosis, first described by Sneddon and Wilkinson [1] in 1955 and introduced to the American literature by Greenbaum and Lee in 1958.[2] Additional cases have been added by Ellis [3] and Shoenfeld,[4] the former writer presenting an extensive review of the literature.

Sneddon and Wilkinson pointed out that this disease complex presents a number of characteristic features which distinguish it from dermatitis herpetiformis, impetigo herpetiformis, pemphigus, and impetigo contagiosa. It is the purpose of this paper to present two patients with subcorneal pustular dermatosis, each of whom displays distinctive features of the disease but whose clinical courses have been very different. In a sense, these patients are at the opposite poles of the spectrum of this disease—the one having purely cutaneous manifestations and responding easily to treatment, the other displaying systemic symptoms and responding poorly to treatment.

CASE 1.—A Negro woman of 25 years was admitted to the Dermatology Department of Henry Ford Hospital, Feb. 14, 1958. In the five days prior to admission she developed pustules, both discrete and grouped, on the chest, neck, trunk, upper arms, forearms, and anteriomedial thighs (Figs. 1 and 2).

For two years scattered pustular lesions had periodically involved these areas. They were accompanied by little or no itching and would heal by desiccation, leaving macular hyperpigmented areas. Her previous treatment consisted of irregular exposures to ultraviolet light and the desultory use of bland lotions. Neither of these treatments was effective.

Submitted for publication Dec. 24, 1958.

From the Departments of Dermatology and Pathology, Henry Ford Hospital. Department of Dermatology (Dr. Burns) (Clarence S. Livingood, Director); Department of Pathology (Dr. Fine) (Robert C. Horn, Director).

Fig. 1.—Case 1; superficial pustules prior to Promacetin therapy.

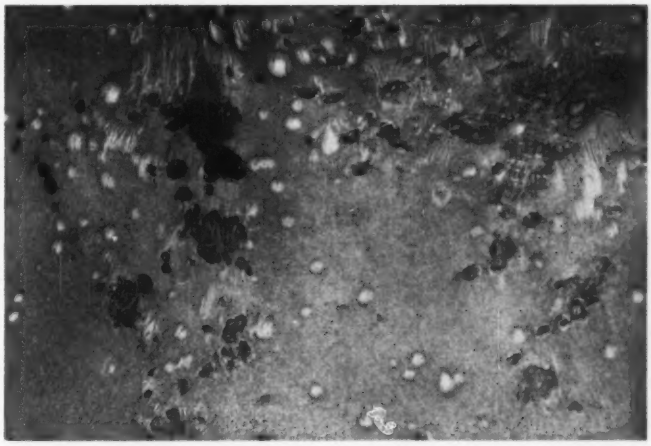


Fig. 2.—Case 1; magnification of Figure 1.

Since July, 1957, she had been under the care of a gynecologist for secondary amenorrhea. He had noticed occasional scattered skin lesions, but these were of so little consequence that the patient did not follow his recommendation to seek dermatologic opinion until the present outbreak occurred.

The patient was afebrile and remained so during the entire period of observation. With the exception of the skin, her general physical examination was normal. Many bullae were found on the skin which varied from several millimeters to several centimeters in diameter. Each lesion was flaccid and extremely superficial and exhibited hypopyon, in which the cloudy material rolled about in the blister, like milk in a Pliofilm bag. Little or no erythema was present about the lesions. There were patches of hyperpigmentation on the abdomen and back, where active lesions had regressed (Figs. 1 and 2).

Laboratory examinations revealed the following findings: hemoglobin 11.4 gm.; WBC 8,500, with band cells 1%, segmented neutrophils 68%, eosinophils 1%, basophils 1%, lymphocytes 22%, monocytes 7%. No immature cells were seen. The red blood cells showed hypochromasia. The platelets were adequate. The N. P. N. was 34 mg. %, and the two-hour postcibum blood sugar, 70 mg. %. The VDRL test was nonreactive. The total protein was 7.2 gm. per 100 cc., with the serum electrophoretic pattern showing albumin 46%, γ-globulin 21%, β-globulin 18%, α_2-globulin 11%, and α_1-globulin 3%. Urinalysis showed a specific gravity of 1.014 acid, albumin negative, Benedict negative, microscopic normal.

Fig. 3.—Case 1; regression of lesions and focal hyperpigmentation following five days of Promacetin therapy.

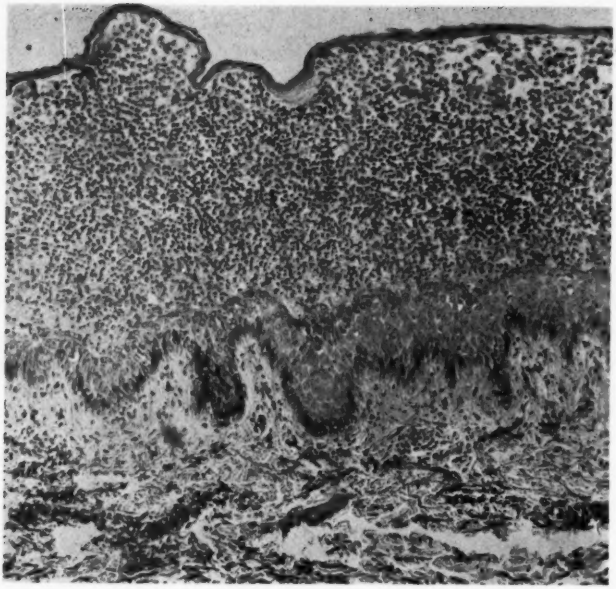


Fig. 4.—Case 1; portion of pustule and underlying dermis with mild perivascular infiltrate. Hematoxylin and eosin; × 105.

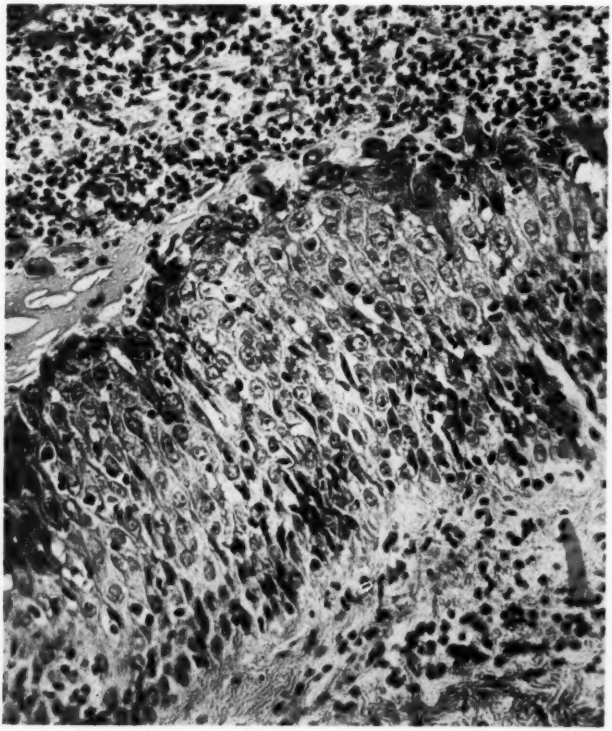


Fig. 5.—Case 1; magnification of Figure 4. Note few acantholytic cells in inflammatory infiltrate. Hematoxylin and eosin; × 300.

Chest photofluorogram showed calcified hilar lymph nodes but was considered unremarkable. Repeated bacterial cultures of pustules were sterile. Fungus cultures on both Littman's and corn meal agar media were negative. Direct smears from the blisters with use of the Tzank technique showed a few round epithelial cells and some polymorphonuclear cells and eosinophils. These blisters were recent but were probably more than 8 to 10 hours old.

Histologic examination: Many sections of a typical lesion revealed an intact pustule situated between the epidermis and stratum corneum, lifting and stretching the latter above the epidermis (Fig. 4). The contents of the pustule were predominantly polymorphonuclear cells with scattered eosinophils and lymphocytes, a small amount of serum, and a rare round superficial squamous cell (acantholytic cell) found at various levels in the pustule either isolated or becoming separated from the epidermis (Fig. 5). The epidermis showed normal pigmentation, moderate acanthosis, and occasional neutrophils. The granular layer was absent in the area of the pustule. No spongiosis or dyskeratosis was found. Minimal superficial acantholysis was present. Minimal perivascular neutrophilic infiltration was found in the upper one-third of the dermis in the area of the pustule. No subepidermal edema was found. Elastic tissue appeared normal with the orcein-azure eosinate stain. Azure eosinate, Grocott, and Brown-Brenn stains were negative for bacteria and fungi. Inclusion bodies were not found.

On the basis of Sneddon and Wilkinson's success with sulfones, the patient was admitted to the hospital and given 0.5 gm. of Promacetin (sodium 4,4'-diaminodiphenylsulfone-2-N-acetylsulfonamide) t. i. d. New lesions ceased to appear, and the old ones dried and desquamated rapidly (Fig. 3). She was discharged on Feb. 22, 1958, with no active lesions, and continued on the above dosage of Promacetin. This was reduced on Feb. 26, 1958, to 0.5 gm. b. i. d. Therapy was discontinued after three weeks, and since that time only an occasional pustule has developed. The lesions left no scar and had almost completely regressed when she was last examined, on May 30, 1958.

CASE 2.—A white woman of 60 years was admitted to the Dermatology Department of the Henry Ford Hospital on Aug. 4, 1958. In 1948, after her husband's death, she developed an asymptomatic bullous eruption of the axillary and inframammary areas which later became generalized. This subsided with the use of an undecylenic acid ointment and potassium permanganate compresses. A year later the eruption recurred in much the same fashion and has varied in intensity and extent since that time. The exacerbations have been greatest in the summer and have been nearly an annual event. They have mainly involved the trunk, arms, and thighs.

Since the onset of the disease the patient had consulted many physicians and had received superficial x-ray treatments, thorium X, streptococcal and staphylococcal vaccines, pantothenic acid ointment, starch baths, potassium permanganate compresses, hydrocortisone ointment, hydrocortisone spray, zinc oxide ointment, ammoniated mercury ointment, various sulfonamides, oral tetracyclines, parenteral penicillin and numerous other antibiotics, potassium arsenite (Fowler's) solution, adrenocorticosteroids, and corticotropin (ACTH). None of these modalities produced more than a transient degree of improvement. Many treatments, including potassium permanganate baths, hydrocortisone spray, and zinc oxide ointment, aggravated the disease. In this period she exhibited hypersensitivity reactions to penicillin, sulfonamides, and potassium arsenite solution.

In 1954, biopsy of the skin was reported by Drs. Wilbert and Perry M. Sachs as follows: "The superficial vessels are dilated and congested and there is interstitial edema of the upper cutis. About the vessels is a focal and somewhat diffuse reaction composed of small round, wandering connective tissue cells, polymorphonuclears and eosinophiles. In some of the sections there is a large subcorneal bullous lesion containing many polymorphonuclears. Otherwise the epidermis shows no important findings. On the basis of routine stain and Hotchkiss-McManus stain, the findings are not those of dermatitis herpetiformis and there is no evidence of any fungi. The picture is that of an impetigo-like lesion and a more specific diagnosis than impetiginized dermatitis cannot be made." Between March and July, 1958, she received immune globulin in doses of 15 to 20 cc. weekly with some temporary benefit. The disease became uncontrollable in July, and she was then admitted to another hospital. Triamcinolone, 40 mg. per day, with corticotropin, 80 units twice weekly, brought the disease under reasonable clinical control. It was soon found that any reduction from this level of steroids would result in a severe exacerbation of the disease within 24 to 36 hours. This consisted of the appearance of multiple areas of cutaneous inflammation, together with a pustular eruption, accompanied by a sharp febrile response. Resumption of full doses of steroids was necessary to control these attacks, which were totally unresponsive to antibiotics. Cultures of the skin were positive before antibiotic therapy, after which they were sterile.

Upon her admission to Henry Ford Hospital, on Aug. 8, 1958, the patient was afebrile and found to have a moderate degree of edema of the face and ankles. Despite the extensive vesiculopustular dermatosis she suffered no discomfort. Dis-

tributed over most of the trunk, arms, proximal two-thirds of the forearms, thighs, and the upper half of the legs were numerous vesiculopustules varying in size from 1 to 12 mm. Some were grouped, but many were discrete. Erythema of the skin was present but not pronounced. There were no excoriations. The palms and soles were uninvolved. The mucous membranes were normal, although several crusted lesions suggesting old vesiculation were found on the lower lip, which were considered herpetic. Areas of hyperpigmentation were observed in a number of areas on the back where active lesions had been present.

Physical examination revealed a woman of 180 lb. whose normal weight was 165 lb. Although the resting blood pressure was 180/80, no evidence of cardiovascular damage was found. The liver, spleen, and lymph nodes were essentially normal, as was the remainder of the examination.

Laboratory examinations revealed the following findings: hemoglobin 12.2 gm.; WBC 10,300, with polymorphonuclear cells 79%, lymphocytes 15%, monocytes 4%, band cells 2%. E. S. R. 49 mm., hematocrit 42%, fasting blood sugar 65 mg. %, N. P. N. 30 mg. %, VDRL nonreactive. The total protein was 5.1 gm. per 100 cc., with the serum electrophoretic pattern showing albumin 2.62 gm. %, α_1-globulin 0.28 gm. %, α_2-globulin 0.85 gm. %, β-globulin 0.74 gm. %, γ-globulin 0.61 gm. %. The thymol turbidity was 1 unit, thymol flocculation 0, and cephalin cholesterol 0. Urinalysis showed a specific gravity of 1.020 and was alkaline, straw color, albumin negative, Benedict negative, microscopic normal. Twenty-four-hour urine collection (1,900 ml.): porphobilinogen negative, coproporphyrin 1+, uroporphyrin negative.

Chest x-ray showed a moderate degree of cardiac enlargement. An oval calcific density, 3×2 cm., was found in the posterior segment of the lower lobe of the left lung. After a review of previous films, this was considered to be a healed granuloma.

Bacterial cultures of bullae on Aug. 5, 7, and 8 revealed Staphylococcus pyogenes var. aureus with an antibiogram showing resistance to penicillin, tetracycline, and erythromycin, and sensitivity to neomycin and Albamycin. Following novobiocin (Albamycin) therapy the cultures were negative.

Dental examination revealed periapical abscesses about the lower left first bicuspid, as well as moderate gingival recession about the lower posterior teeth and all of the upper teeth.

Histologic examination: Biopsy of a pustule on the forearm (Aug. 13, 1958) revealed changes similar to those of Case 1 (Figs. 6 and 7). Azure eosinate, Grocott, and Brown-Brenn stains were negative for fungi and bacteria. Cellular inclusions were not seen.

Course: Throughout her hospital course the patient was remarkably comfortable despite the severity of her disease. A few new pustules surrounded by an inflammatory reaction of greater degree than previously observed appeared on Aug. 6. After bacterial culture was obtained, erythromycin, 250 mg. per os. q. i. d., was prescribed. The inflammatory reaction continued to increase, and on Aug. 8 erythromycin was discontinued and

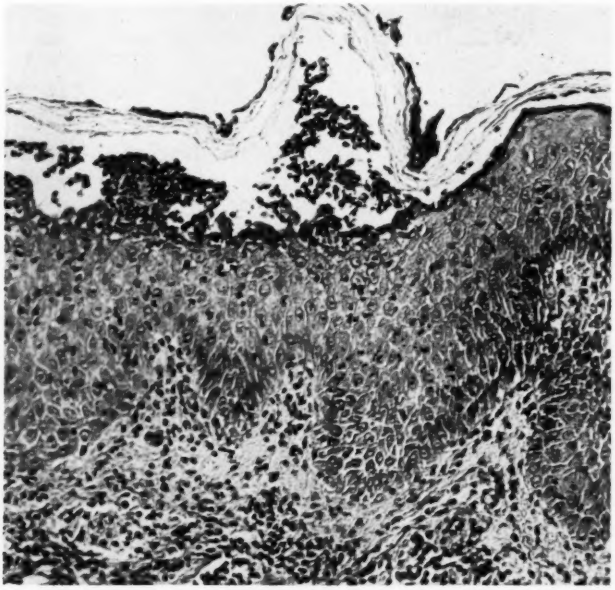


Fig. 6.—Pustule of Case 2. Hematoxylin and eosin; ×170.

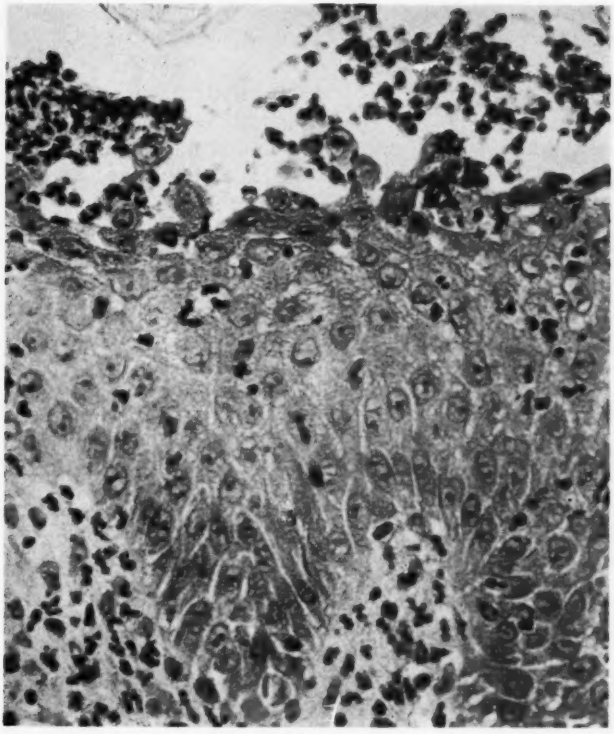


Fig. 7.—Case 2. Minimal and superficial acantholysis in contrast to that of pemphigus (Figs. 8 and 9). Hematoxylin and eosin × 450.

novobiocin stated in the same dosage, after the receipt of a bacteriologic report that the S. pyogenes var. aureus infecting the skin was resistant to erythromycin and sensitive to novobiocin. Blisters continued to appear the next day, and 40 mg. prednisolone daily was instituted in addition to the antibiotic therapy. Within 24 hours resolution of the eruption was evident.

On Aug. 11, after the extraction of the first and second lower left bicuspid teeth, novobiocin was discontinued. Numerous grouped superficial flaccid pustules, which proved to be sterile, developed on the back and forearms on the following day. A diagnosis of subcorneal pustular dermatosis was established on the basis of the clinical appearance and biopsy findings. Because of the patient's known sulfonamide sensitivity, nicotinic acid, 100 mg. t. i. d., and potassium arsenite solution, 3 drops t. i. d., were prescribed, together with a very gradual diminution in the dosage of prednisolone. The eruption slowly improved and continued its regression after her discharge from the hospital on Aug. 17. She returned to her home and to the supervision of her physician eight days later. Since then she has remained on maintainence doses of 15 mg. prednisolone per day and ancillary supportive treatment, together with nicotinic acid. Her skin, at this dose level, continues to display diffuse erythema and occasional superficial pustules. When the dose of prednisolone is lowered, the skin becomes grossly inflamed and many pustules appear.

While this patient was under our care, it became apparent that she was a competent person who demanded a great deal of herself. This drive had been apparently accentuated by her husband's death and by the associated responsibilities she was obliged to accept. One cannot assess the relationship of this observation to the disease, except to note that the eruption appeared at the time of the death of her husband.

Comment

The disease in Case 1 was of moderate severity and was easily controlled. The lesions were largely confined to the upper trunk, arms, and neck. The subcorneal location of the blisters were diagnosable at a glance. Itching was absent; there were no systemic signs or symptoms, and her

response to Promacetin was dramatic. The future course of her disease is, of course, unpredictable.

Case 2 represents the opposite end of the spectrum. Here the patient was disabled by the chronic, widespread eruption which in many respects mimicked dermatitis herpetiformis of the severe variety. The absence of pruritus was remarkable and perhaps should give one a clue to the nature of the process. The presence of subcorneal pustules in 1954, we believe, makes it highly unlikely that the pustules which appeared during the course of her most recent hospital admission were superficial because of the influence of treatment. The infection of her skin, present early in her recent hospital stay, could have produced subcorneal blisters of the order of those seen in impetigo contagiosa bullosa, but the bullae continued to appear after all infection had subsided under appropriate antibiotic therapy. Her disease continues unabated, suppressed only by steroid therapy.

While clinical characteristics might allow the differentiation of subcorneal pustular dermatosis from other bullous eruptions, definitive classification still awaits microscopic and cultural examinations. From a histologic point of view pemphigus and impetigo contagiosa bullosa would be the diseases with which there might be some confusion. Although pemphigus does not generally have subcorneal lesions, occasional areas may show an infiltrate similar to that seen in subcorneal pustular dermatosis (Figs. 8 and 9). Differentiation can be made, however, on the large number of acantholytic cells in the pustule of pemphigus and on the depth of the acantholytic process in the epidermis beneath and adjacent to the pustule.

The histology of impetigo contagiosa bullosa and that of subcorneal pustular dermatosis may be identical. Differentiation between the two is dependent upon clinical differences and the presence of bacteria in the former. Although free epithelial cells may be found in the pustules of both subcorneal pustular dermatosis and impetigo, they are not as numerous as in pemphigus. Their presence in the former two may be explained by the proteolytic action of the pustular contents on the superficial epithelium [5] rather than an acantholytic process as seen in pemphigus.

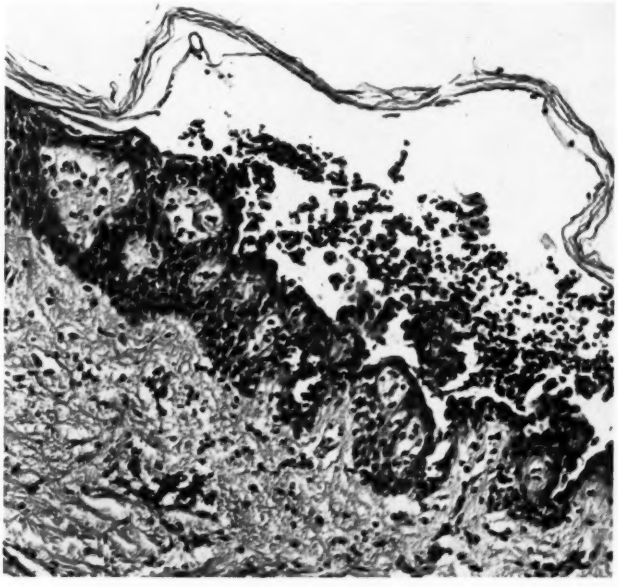


Fig. 8.—Pemphigus with superficial pustule resembling those of sub-corneal pustular dermatosis. Hematoxylin and eosin; × 170.

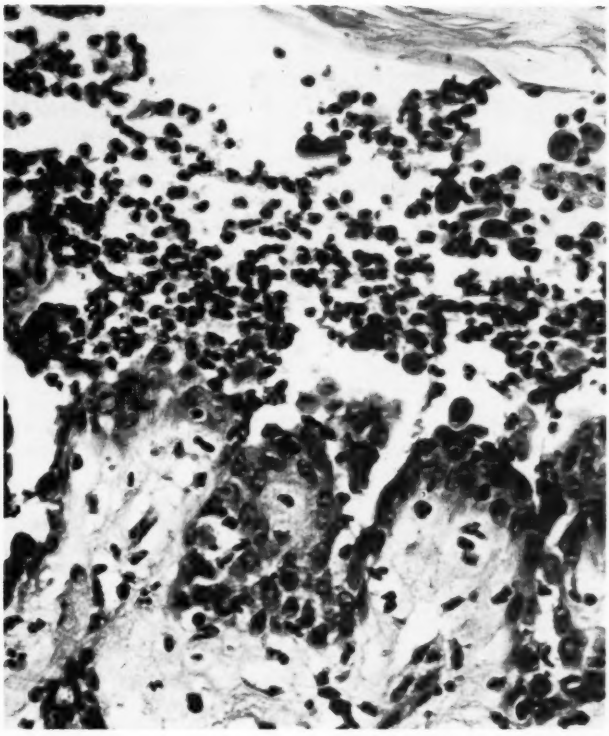


Fig. 9.—Magnification of Figure 8. Note abundance of acantholytic cells and depth of acantholysis in epidermis in contrast to subcorneal pustular dermatosis. Hematoxylin and eosin; ×450.

Other bullous eruptions, such as pustular psoriasis, acrodermatitis continua, pustular bacterid, impetigo herpetiformis, and pemphigoid, are more pathologically distinct from subcorneal pustular dermatosis. Distinction from dermatitis herpetiformis and its many variants is simple enough in typical cases but in problem cases awaits histologic examination of a characteristic blister, as in our Case 2.

In subcorneal pustular dermatosis there is little or no pruritus. The patients are almost invariably women and have generally been reported in the 40- to 70-year age group. The eruption has not yet been described in the mucous membranes. It is mainly distributed over the flexures, especially the axillae and the groins; the proximal portion of the extremities, and the trunk. As in dermatitis herpetiformis, the course is frequently a protracted one and may be of varying degrees of severity. Also as in dermatitis herpetiformis, the consistent coincidence of focal or systemic disease, while frequently sought, is rarely found, although Hellier's patient,[6] a man, had associated lesions of pustular bacterid involving the soles for a number of years prior to the appearance of the subcorneal pustular dermatosis on the trunk and extremities. Again, like dermatitis herpetiformis, subcorneal pustular dermatosis usually responds well to the use of the sulfone group of drugs, yet, unlike dermatitis herpetiformis, it is not predictably responsive to the administration of sulfapyridine.

Until more is known of the etiology of subcorneal dermatosis and, in fact of the other bullous diseases, one is obliged to keep an open mind regarding the basic processes concerned with their production. On the basis of the characteristic cellular pathology one can separate the true

acantholytic diseases from those failing to show acantholysis. The nonacantholytic bullous diseases, such as epidermolysis bullosa, porphyria, erythema multiforme, bullous lichen planus, pemphigoid, and dermatitis herpetiformis, each have certain microscopic characteristics but are mainly separated by their concomitant clinical and at times metabolic peculiarities. The extreme variability found in the clinical and pathologic pictures of these eruptions leads one to be somewhat circumspect in considering subcorneal pustular dermatosis to be a new entity. Its variance from other members of the nonacantholytic group (especially the broad syndrome of dermatitis herpetiformis) may simply represent a difference in tissue response to stimuli similar to those producing these latter diseases. However, its clinical and pathological features are reasonably separable from the other bullous diseases, and for the time being we believe that subcorneal pustular dermatosis is a diagnosable entity and that its diagnosis serves a useful purpose even though it seems closely related to dermatitis herpetiformis.

Summary

Two cases, presenting pustular lesions clinically and histologically similar to the recently described subcorneal pustular dermatosis, are presented. Although there may be a superficial clinical or histologic similarity between it and other bullous and pustular eruptions, we feel histologic examination justifies its separation from the previously described pustular and bullous eruptions.

Department of Dermatology, Henry Ford Hospital (2).

REFERENCES

1. Sneddon, I. B., and Wilkinson, D. S.: Subcorneal Pustular Dermatosis, Brit. J. Dermat. 68:385, 1956.

2. Greenbaum, C. H., and Lee, J. B.: Subcorneal Pustular Dermatosis, A. M. A. Arch. Dermat. 77:512, 1958.

3. Ellis, F. A.: Subcorneal Pustular Dermatosis, A. M. A. Arch. Dermat. 78:580, 1958.

4. Shoenfeld, R. J.: Subcorneal Pustular Dermatosis, A. M. A. Arch. Dermat. 78:589, 1958.

5. Stoughton, R. B.: Mechanisms of Blister Formation, A. M. A. Arch. Dermat. 76:584, 1957.

6. Hellier, F. F.: Generalized Pustular Bacterid: Its Relationship to the Pustular Dermatosis of Sneddon and Wilkinson, Brit. J. Dermat. 68: 395, 1956.

Lichen Planus-like Eruption Caused by Color Developer

ORLANDO CANIZARES, M.D., New York

The development of lichen planus-like eruptions following medications is common. Gold, arsenic, and quinacrine (Atabrine) are capable of eliciting this type of cutaneous reaction. The lichen planus-like eruptions discussed in this paper appear to differ from those previously reported in that they developed after external exposure to a chemical agent which was not a drug.

On Feb. 5, 1958, I had the opportunity of examining a patient presenting an extensive eruption, with residual pigmentation of the hands, forearms, neck, and face. It consisted of pinhead-sized, flat, shiny papules, clinically suggestive of lichen planus. A biopsy confirmed this diagnosis. This patient was engaged in processing color film in a plant in New York City, and he attributed the eruption to his work. Since the diagnosis of lichen planus had been confirmed by histologic examination, the disease was not initially considered as of occupational nature. However, within two months, I saw four more patients from the same plant, all presenting the same clinical picture, a lichen planus-like eruption, and in addition all were engaged in processing color film. The history given by all patients was significantly suggestive of an occupational relationship.

A careful search of pertinent literature failed to disclose any similar cases, despite the fact that color photography is not a recent development.

Submitted for publication Nov. 11, 1958.

From the Department of Dermatology and Syphilology of the New York University Post-Graduate School (Dr. Marion Sulzberger, Chairman) and the Service of Dermatology and Syphilology of Bellevue Hospital (Dr. Frank C. Combes, Chief of Service).

Seeking information on this matter, I wrote to Donald J. Birmingham,[1] Medical Director of the Occupational Health Field Headquarters, Department of Health Education and Welfare. He answered that approximately a year previously he had been informed of this type of eruption by Buckley, Consulting Dermatologist of the Eastman Kodak Company, and he suggested that I write to the latter for further information. In his answer, Buckley[2] quoted directly from a paper which, he stated, had been recently submitted to the A. M. A. ARCHIVES OF DERMATOLOGY.

I have also received communications from Shaw[3] and Hallett,[4] of Rochester, N. Y., Sheard,[5] of Stamford, Conn., and through Donald Birmingham from Osorio,[6] of Mexico City, all of whom report similar cases. In these independent observations, the dermatologists invariably emphasized the lichen planus-like eruption and its high incidence among workers processing color film by one particular method. No cases have been observed in the persons engaged in color processing by other methods.

One of my patients was presented at the meeting of the New York Dermatological Society in April, 1958. In the discussion, Dr. Domonkos stated that, with Dr. Andrews, he had recently observed a similar case.

Clinical Picture

Two entirely different clinical pictures may be observed in the persons engaged in the processing of color film: an acute, eczematous, contact type dermatitis and a subacute or chronic lichen planus-like erup-

tion. Both, although usually independent, may coexist; or the eczematous type may gradually develop lichenoid lesions. Conversely, patients with the latter type of eruption may develop, on rare occasions, acute eczematous lesions.

In my experience, the acute eczematous contact type dermatitis is encountered in the minority of patients. Its clinical appearance does not differ from that caused by any other contactant. Erythema, edema, and vesiculation with resulting crusting and possible secondary infection are usually observed. The security of the symptoms depends primarily on the sensitivity of the patient and the amount of exposure.

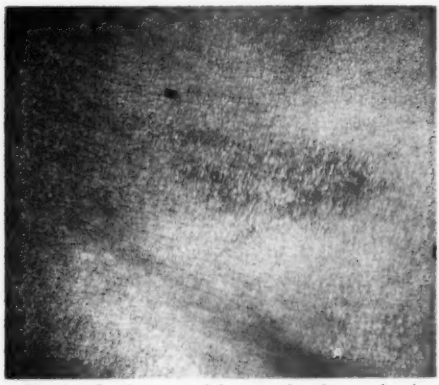


Fig. 1.—Lesions on abdomen, showing a clearing in the center with active minute lichen planus-like lesions at the periphery (print from a color transparency).

Fig. 2.—Tissue sections from a lichen planus-like lesion, showing an acanthotic and flattened epidermis, granular and horny layer increased, and washing out of the basal-cell areas.

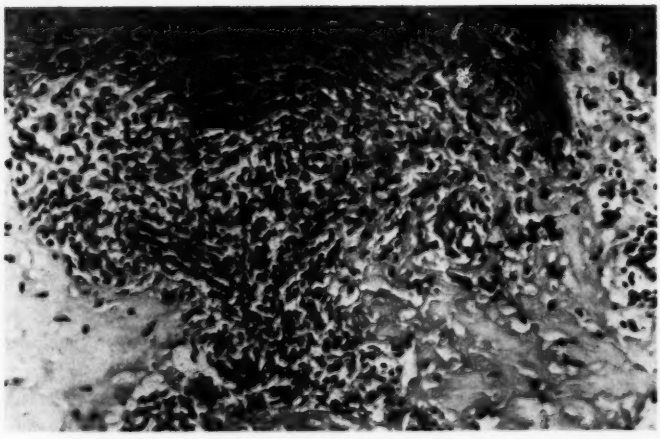


Fig. 3.—Band-like infiltration with small, round, and connective tissue cells.

In the severest cases, who were apparently extremely sensitive, even a minimal contact caused by minute particles of the chemical suspended in the air seemed sufficient to cause pronounced itching and erythema.

The clinical course of the acute eczematous type is similar to that due to other contactants. Under appropriate treatment, provided further exposures are discontinued, the lesions resolve. Recovery is, as a rule, slow and necessitates the usual routine therapeutic procedures. Cases with severe inflammatory edema and vesiculation may require hospitalization. Corticosteroids are helpful in these patients.

Further contact usually results in relapses, the severity determined by the degree of exposure. In some cases, after the acute process has subsided, minute lichenoid papules may appear in the areas of residual pigmentation.

The second type, the subacute or chronic lichen planus-like eruption, is by far the commonest. The expression "lichen planus-like" is preferred, as it is more descriptive than the vague term "lichenoid," which customarily is used to designate papular eruptions, often flesh colored, slightly erythematous, or even translucent.

In their early stages the lesions are punctate to miliary angulate, flat papules. The surface is smooth and shiny; the color varies with the color of the patient's skin, from reddish purple to purplish brown or even slate. On magnification, in some instances, whitish puncta and striae identical with Wickham's striae are seen. The lesions, therefore, present all the clinical features observed in lichen planus.

As the disease progresses, the isolated papules coalesce, forming irregularly shaped patches. They may cause heavily infiltrated, verrucous, and hypertrophic plaques.

No involvement of the oral mucosa was seen. Residual pigmentation was noticed on the glans penis, and annular lesions were present in one patient on the shaft of the penis. In more advanced cases following involution of the papules, the affected areas were pigmented, sepia to blackish hue, depending on the previous color of the skin. In the Negro this hyperpigmentation was intense black. Often within this residual hyperpigmentation pinpoint- to pinhead-sized papules could be detected.

The distribution of the eruption is characteristic and helpful in diagnosis. It usually extends from the tip of the fingers, dorsally, to the elbows or even the shoulder. The entire surface of the forearms, both flexor and extensor aspects, may be involved. The papules are frequently closely packed and may form an uninterrupted patch, but more often there are patches of a few centimeters in diameter with normal skin between. On the flexures of the elbows there may be parallel lines of papules along the normal wrinkle lines over the joint.

The eruption is bilateral and symmetrical, the upper extremities being the commonest location. The sides of the neck and face are also often affected. The eyelids are possibly affected by direct application of the chemical from the hands. The same may be said of the penile lesions. Lesions on the trunk and inner aspect of the thighs were often observed. On the thighs peculiar reticulate and vague annular patterns occurred in one patient.

The subjective symptoms varied. The patients with lichen planus-like lesions had little or no pruritus. However, they stated that during the early stages of the eruption itching was intense. In some instances pruritus preceded the eruption, suggesting a subclinical stage of dermatitis.

The course of the lichen planus-like eruption is gradual and protracted. Six months or a year after its onset the patient may continue to develop new lesions in previously unaffected locations. The pruritus, very severe at the onset, gradually subsides.

Incidence

The incidence of the eruption among workers exposed to the agent is quite high. In my series from a small plant, five cases were observed in four months; this was the majority of the operators engaged in this

type of work. Recently additional cases have occurred. Shaw [3] states that he had observed about 20 cases in one year from small plants in Rochester, N. Y. Sheard [5] reports six cases in Stamford, Conn. In Osorio's [6] series, in Mexico City, about one-half of the workers engaged in the processing of color film were affected.

Pathogenesis

The contact dermatitis and the lichen planus-like eruptions observed in persons engaged in the processing of color film by the one particular method appear to be due to ingredients contained in a color developer preparation. Since this is a patented formula, the independent investigator is placed at a disadvantage as to the exact nature of the responsible ingredients. Buckley [2] referred to them as "the hydrochloride salt of the substituted *p*-phenylenediamines." He further stated that the particular chemical is related to aminosalicylic acid, which was reported by Shatin, Canizares, and Worthington [7] as a cause of lichen planus-like eruptions when taken internally in the treatment of tuberculosis. Possibly additional ingredients used in the complex combination of chemicals used in the process may also contribute to the dermatitis.

Most workers stated that they came in direct contact with the solution in the process of developing color film. They explained that while working in the darkroom it was necessary to immerse their hands in tanks containing the solutions to rescue broken films or to correct other irregularities. In other instances, the direct contact was due to the developer dripping from the racks containing films after their removal from the tanks. In other patients, in the preparation of the solutions the mixing of the powder color developer with other dyes caused an air-borne dermatitis. Most darkroom workers also prepare solutions.

Shaw [3] reported that his severest case occurred in a janitor whose job was to pick up the scrap film and who was not exposed directly to the developing solution.

It is possible that two mechanisms are involved. It seems logical to assume that, since the lichen planus-like eruptions appear primarily on exposed areas, with or without a preceding dermatitis, their development is directly due to a local sensitizing action of the chemical on the skin. It is unlikely that all lesions can be explained on a basis of environmental contact.

Although most lichen planus-like lesions affect exposed areas, there is enough evidence to suspect absorption as a possible explanation of the retiform and annular lesions appearing on the trunk, inner aspect of the thighs, and penis. The pattern of these lesions would be difficult to explain on a contact basis and is almost incontrovertibly indicative of internal origin. Inhalation or ingestion of food accidentally contaminated by the hands of the worker may possibly play a role in the internal dissemination of the allergen.

An interesting feature was observed by Osorio. He studied a patient who had, prior to employment as a color developer, suffered from a lichen planus. When in contact with the color developer the patient experienced an exacerbation of his original eruption. This would indicate that further study of these eruptions may be of help to us in understanding the etiology of lichen planus.

Pathology

The histologic picture of the lichen planus-like eruption caused by the chemical agent in question was studied by Wilbert and Perry Sachs. In their findings they reported an acanthotic and flattened epidermis, granular and horny layer present and increased, and washing out of the basal-cell areas. Some sections showed small spaces between the infiltration and the epidermis, suggestive of a Max Joseph lacuna. The infiltration is band-like ,of small, round, and connective tissue cells and chromatophores. About the vessels there is simple cell reaction and chromatophores. They concluded that the findings are those of lichen planus. In other sections, they de-

scribed a lichenoid dermatitis showing features of lichen planus and stated that this picture can be caused by a drug.

Patch Tests

Patch tests with the above-mentioned color developer solution give a positive reaction on most patients. These are of the usual vesicular eczematous type and pruritic, and they last for several days. Bullous reactions have been observed, especially in patients presenting the acute type of dermatitis. In performing the patch test, it should be kept in mind that in actual working conditions the color developer is mixed with other solutions used in the processing of color film, and so a positive reaction to the solutions handled by the worker, possibly other dyes, and referred to by them as "cyan," "magenta," and "yellow" does not necessarily indicate a sensitivity to these agents.

The response to patch tests is not as uniform as might be expected. Shaw [3] stated that they were extremely variable, some presenting an eczematous reaction, while others had a negative response. He also stated that one of the severer cases had a strongly positive eczematous reaction to the processed color film but none to the undeveloped color film.

Lichen planus-like lesions have not been reproduced by patch test by Shaw, Shear, or myself. Buckley states, "The hydrochloride salt of the substituted *p*-phenylenediamines when applied to the skin of a sensitized operator will reproduce an eruption which evolves to duplicate the lesions seen clinically." Possibly a long follow-up observation of some of those presenting a positive patch test may detect the development of a lichen planus-like reaction at the site of the test.

The lack of uniformity observed in the patch tests may possibly be explained by the immunological status of the patient. Some may have developed a "hardening." It may be possible that the development of lichen planus-like lesions represents a higher degree of resistance of the individual patient.

Prophylaxis

The prevention of this dermatitis is paramount. Apparently, in most cases, this has failed, as may be judged by the high incidence of cases observed among those exposed. Buckley states that the main impetus of the physicians who have observed these eruptions for over 30 years was directed toward the prevention of the lesions and not to their description. Judging from this high incidence after three decades of study, it is deplorable that more is not known regarding the pathogenesis and prophylaxis. Buckley [2] states that a discussion of its prevention was included as part of the course given by the sales division of the firm using this color developer for photofinishers not working for that company.

Some procedures have been suggested to reduce the incidence of this industrial hazard. The actual handling of the solutions and the powders with which they are prepared should be reduced to a minimum. The use of gloves has not proven practical, as it decreases the dexterity of the worker and really does not afford adequate protection. Facilities to wash the worker's hands inside the darkroom are essential. Frequent washing will also reduce the possibility of accidental ingestion of the chemical. Shaw [3] recommends the use of Phisoderm (a synthetic skin detergent) or immersion of the hands in diluted acetic acid. This seems to counteract the severity of the reaction, since the solution is alkaline. The usual protective creams, with or without silicone, have not been effective.

In view of the possibility that inhalation may be responsible, proper ventilation and exhaust fans should be installed in all darkrooms.

Obviously the most effective preventive measure will be to avoid actual handling of the solutions. The use of closed machines, capable of doing the work auto-

matically, would certainly be the simplest solution from an industrial standpoint.

Summary and Conclusions

Persons engaged in the processing of color film by one particular method are exposed to chemicals in different developing solutions which may cause sensitization dermatitis. One of them, apparently contained in a color developer preparation, seems to be highly sensitizing. The exact nature is covered by a patent. It has been described by Robert Buckley,[2] dermatologist of Eastman Kodak, as a "hydrochloride salt of the substituted *p*-phenylenediamines."

This agent apparently may cause an acute eczematous contact type dermatitis and a subacute or chronic eruption which is clinically and histologically identical with lichen planus.

The lesions appear from a few weeks to several months after exposure to the agent. Direct contact with the solution is the commonest cause. Airborne contact with the powders while the solutions are being prepared may also be the sensitizing mechanism. Apparently enough chemical remains in the freshly developed film to cause sensitization, as evidenced by the case of Shaw[3] in a janitor who became sensitized by picking up scraps of developed film.

The distribution of the eruption is rather characteristic: bilaterally symmetrical involvement of the hands, with angular, shiny, smooth papules, varying in color from reddish purple to purplish-brown or slate color. Extension to other areas, where the eruption sometimes presents an annular or reticular configuration, suggests the possibility of absorption of the chemical through the skin, lungs, or gastrointestinal tract.

The incidence of the eruption is high; in some instances the majority of workers in a small plant become affected.

Patch tests with the color developer usually give a positive reaction of the eczematous type. Negative reactions too are seen, especially several months subsequent to onset of the eruption. This may indicate a development of a "hardening" process.

The most important preventive measure is avoidance of contact with the agent. Other measures, such as gloves, protective creams, etc., have failed.

The observation by Osorio of a patient whose "true" lichen planus was reactivated by exposure to the chemical agent is significant and should stimulate inferential reasoning.

The development of an eruption, which clinically and histologically resembles lichen planus, after exposure to a chemical agent opens a new field for research in the study of the etiology of this disease.

3 E. 69th St. (21).

REFERENCES

1. Birmingham, D. J.: Personal communication to the author.

2. Buckley, R.: Lichenoid Eruptions Following Contact Dermatitis, A. M. A. Arch. Dermat. 78:454 (Oct.) 1958.

3. Shaw, H. C.: Personal communication to the author.

4. Hallett, J.: Personal communication to the author.

5. Sheard, C.: Personal communication to the author.

6. Osorio, F. R. F.: Personal communication to the author.

7. Shatin, H.; Canizares, O., and Worthington, E. L.: Lichen Planus-like Drug Eruption Due to Para-Amino Salicylic Acid, Invest. Dermat. 21:135-138 (Sept.) 1953.

A Case for Diagnosis, by Geoffrey Chaucer (1340?–1400)

MARC WEINER, M.D., Washington, D. C.

From General Prologue, "The Canterbury Tales."

A Somnour was ther with us in that place,
That hadde a fyr-reed cherubinnes face,
For sawceflem he was, with eyen narwe.
As hoot he was, and lecherous as a sparwe,
With scalled browes blake, and piled berd;
Of his visage children were aferd.
There nas quik-silver, litarge, ne brimstoon,
Boras, ceruce, ne oille of tartre noon,
Ne oynement that wolde clense and byte,
That him mighte helpen of his whelkes whyte,
Ne of the knobbes sittinge on his chekes.
Wel loved he garleek, oynons, and eek lekes,
And for to drinken strong wyn, reed as blood.

Translation

A Summoner* was with us in that place
That had a fiery-red cherubic face,
For pimpled all he was, with eyes narrow.
As hot he was and lech'rous as a sparrow,
With black brows scabby and a scanty beard;
And of his visage children were afeard.
There was no mercury, white lead, brimstone,
Borax, ceruce† nor cream of tartar none;
Nor any ointment that would cleanse and bite,
That ever might help him of his boils white,
Or of the knobs that sat upon his cheeks.
Well loved he garlic, onions, also leeks,
And for to drink strong wine as red as blood.

915 19th St. N. W. (6).

Submitted for publication Nov. 4, 1958.

* Summoner to ecclesiastical courts.

† An ointment containing white lead.

Reports

A Dermatologist's Trip to Japan*

STEPHEN ROTHMAN, M.D., Chicago

The first and most striking experience after my arrival in Japan was the overwhelming friendliness and superb hospitality of my hosts. They planned and executed all minute details of my program so as to make my stay pleasant and comfortable. From the beginning until the end, I had alternately three young dermatologists assigned to me as escorts. These wonderful young men, A. Kukita, M. Miyamoto, and J. Fan, had worked previously in the United States with Tom Fitzpatrick, Hermann Pinkus, and Ray Suskind, respectively, and speak fluent English. They not only took care of my travel schedules, taxis, trains, sightseeing, and custom inspections but helped me to pack and unpack, delivered and picked up my laundry, mailed my letters, and helped me to shop. In the little time left after all these personal services were performed, they worked feverishly on the translations of my lectures. The older and higher ranking professors were equally considerate, concerned about my well-being and comfort and took care continuously of dining, wining, and entertainment. Everywhere I was showered with beautiful gifts, most of them skillfully bundled by the presenter in artistic and colorful silk cloth.

The second great impression was the beauty of the countryside. Traveling from Tokyo to Niigata the train took us through wooded mountains and narrow winding valleys with torrentous streams at the deep bottoms. The landscape reminded me of the beauty of my early stamping grounds in the Drave Valley in Carinthia. Similarly, the landscape of the hilly Eastern Range of Kyoto and Nara was overwhelming.

The Japanese gardens, in public parks, historical sites, museums, hotels, and homes are another source of delight. They are man-made sublimations of natural beauty. The top of "gardening art" is the road to Nikko, lined by 700-year-old Japanese cedar trees and surrounded by forests of azalea trees.

Submitted for publication April 17, 1959.

* Special Report.

Dr. Rothman delivered the first Dohi Memorial Lecture, May, 1958.

Section of Dermatology, Department of Medicine, The University of Chicago.

Among other products of art the masterworks of Japanese landscape painting are relatively best known in the Western world. They are indeed lofty summits of artistic creation. Another peak achievement of artistry is Japanese porcelain. I was particularly impressed with the purple-red procelain, the secret formula of which was relayed from generation to generation in the Kakiemon family in the 17th century. Among architectural works, the pagodas in large gardens are a lovely sight. Other architectural decorations, however, as well as theater, puppet theater, music, and the singing and dancing art of the geishas are so strange for the Western visitor that probably they require more thorough study to be recognized as great works of art.

Westernization is rapidly progressing in the large cities of Japan. However, the traditions in family life, social habits, social structure, and professional and business life in Japan have been so vastly different from those of the West that a struggle between deep-rooted traditions and modernization is felt everywhere and often painfully so. This is particularly true for young men and women pursuing a career in medical and other sciences who have spent more or less time in the States or elsewhere in the West. The most painful contrast is the rather subdued role of women, who still hardly ever take part in the social life of men.

As to dermatology, I was greatly impressed with its high standing in Japan, in both its clinical and its investigational aspects. They abound in first-class clinicians, e. g., S. Kitamura, T. Kobori, O. Miura in Tokyo, T. Yamamoto in Kyoto, Y. Sakurane, and T. Fujinami, in Osaka, and many others. They have the ability of sharp discrimination and a clinical acumen just like the best ones in Europe and in our own circles.

I attended three major clinical sessions with patient demonstrations. With courteous regard to the visitor many cases were shown which are characteristic for the Japanese scene, among them peculiar keratotic and pigmentary anomalies, such as keratodermia tylodes palmaris progressiva (Dohi-Myiake), dyschromatosis symmetrica hereditaria (Toyama), acropigmentatio reticularis (Kitamura), keratosis follicularis squamosa (Dohi), pityriasis circinata (Toyama), and a great

number of cases with nevus Ota. Severe tuberculids of the penis (papulonecrotic type) seem to be remarkably common in Japan. Melanosis of Riehl is a frequent diagnosis. Two types are distinguished: a lichenoid hyperkeratotic reticular type which responds to arsenical therapy and a diffuse type not responding. There were interesting case reports of systemic infections with dermatophytae (e. g., Trichophyton rubrum invading the brain) and unusual cases of sporotrichosis, chromoblastomycosis, etc. "Modern" diseases also were shown, such as leukomelanoderma from use of hydroquinonemonobenzylether.

The mechanics of patient presentation are less handy than in this country. Mostly, the patients cannot be inspected in advance but are shown in large auditoria in sitting position, not adequately undressed, and the light is sometimes poor. The young men in the last rows hardly dare to come forward to see the patient. On the other hand, we can learn a lot from our Japanese colleagues when it comes to projection of excellent colored clinical and microscopic photographs of the case under discussion.

A symposium on "eczema," its classification, pathogenesis, and treatment, offered a peculiar mixture of old-fashioned or even antiquated and modern viewpoints. I could follow the discussion, although held in Japanese, because of the numerous comprehensive slides with English inscriptions. Obsolete classification principles, such as different lichenoid dermatitides of the Vidal, Brocq, Besnier, and Devergie type, were revived. These, of course, included lichen Vidal, atopic dermatitis, and also nummular eczema of our terminology, but, according to modern principles, eczematous contact dermatitis and seborrheic dermatitis were treated as separate entities. As I gathered from *ad hoc* whispering translations and the laughter of the audience, the discussers were witty, particularly M. Ito, the prominent melanin expert.

Therapeutic methods, in general, are similar to those used in America and in Europe. S. Ishizu, of Toho University, reported on a fluorescent photosensitizing carbohydrate-protein complex extracted from pseudomonas, "I. I. G.," which several Japanese authors find much more effective in the treatment of vitiligo than the psoralens. The results, indeed, seem encouraging. In other instances, however, some of the therapeutic enthusiasm seems to be precocious because of lack of controls. For instance, the intratumoral injections of vaccinia virus into warts and skin cancers seems to act by necrotization, and I wonder how elective this effect is. The effect of some drugs on the course of alopecia areata recommended for its treatment seems to me to be indistinguishable from spontaneous cure, but, alas, we find early therapeutic enthusiasts all over the world!

In syphilology our Japanese colleagues are remarkable experts, as it can be expected in the country of the great Dohi, the grand old master of clinical syphilology; S. Matsumoto, of experimental syphilology, and T. Ogata, of serology. I had the honor and pleasure to meet Professor Matsumoto, in Kyoto, and Professor Ogata, in Tokyo.

As always and everywhere, in Japan, too, war and military defeat were hotbeds for the spread of syphilis. The sources of infection could not yet be brought well under control, in spite of the availability of penicillin, mainly because of lack in the control of prostitution. Syphilologists hope that the newly passed Anti-Prostitution Act will help.

K. Takenouchi, Chiba University, gave a thorough analysis of seroresistance after a follow-up for many years of 130 syphilitic long-term prisoners. He found that patients who in the early period showed very high serologic titers were most likely candidates for seroresistance.

There are 15,000 leprosy patients in Japan, as contrasted with 30,000 in 1904. I visited the National Leprosorium, Zama Zensho-En, near Tokyo, a 50-year-old institution which had been gradually enlarged but hardly modernized. At present it has a capacity for 1,570 patients. It spreads over 97 acres and the patients are living in 257 houses, all surrounded with pretty gardens. The houses are extremely simple but scrupulously clean wooden structures. In addition, there are hospital buildings for the acutely ill. Strangely enough, in some wards the sexes are not separated. There are facilities for agricultural work, all kinds of handicraft, and sport facilities. Among the 32 full-time resident physicians, all specialties are represented. The medical care is at highest modern standards. The plastic surgeon, who happened to be my guide through the premises, showed me marvels in reconstruction of mutilated ears, noses, hands, and feet. Seventy per cent of the patients had lepromatous leprosy, but only twenty per cent were active. The preferred sulfone preparation is glucosulfone (Promin); sulfoxone (Diasone) is thought to be less effective. I saw one remarkable case of small-papular lepromatous leprosy of the face, clinically indistinguishable from lupus miliaris disseminatus faciei.

Concerning investigational aspects I first should like to mention the magnificent conference on sweat physiology which was arranged by the dean of Japanese physiologists, Y. Kuno, in Kyoto. Because of the outstanding work of Kuno and his school, the Japanese have been leading in this branch of physiology for many years. Recently, M. Wada, at Tohoku University, in Sendai, has made significant contributions in the field. Our conference was to my knowledge the first confer-

ence entirely devoted to the physiology of sweating in the history of sciences.

Ten short experimental papers were presented, all read in English. Our basic-science colleagues are definitely more polyglot than the clinicians. The presentations were in the American style of the Federation meetings. The subjects were effects of sleep, of pressure, and of different autonomic drugs on reflex sweating, chloride concentration of skin tissue, histochemistry and electron microscopy of sweat glands, and relation of sebaceous excretion to sweating. The climax was Kuno's presentation of a new hypothesis on the evolutional development of the sweat apparatus. In brief, it is assumed that originally all sweat gland nerves were adrenergic. Cholinergic fibers developed gradually and reached in man a perfection enabling the sweat glands to discharge enormous amounts of water. The adrenergically innervated (apocrine) glands of mammals have gradually undergone a natural denervation and at the same time acquired great sensitivity to epinephrine and norepinephrine (arterenol). When horses, donkeys, sheep, and goats sweat during exercise, this is due to humoral norepinephrine stimulation.

A most impressive piece of investigative work is that of Nishiura, University of Kyoto, on tissue cultures of lepromatous nerves and electron microscopy of the lepra bacillus. His findings enabled him to reconstruct the natural history of invasion of tissues by the bacillus and of the reactions of this invasion. His associate, Imaeda, has used modern histochemical methods in the study of tissue enzymes in leprosy.

J. Yamazaki, Gumma University, presented a beautiful paper on physiology of itching with the novel finding of intraepidermal nerve endings in palms and soles. Y. Okuno, Kurume University, discussed interesting ideas on the nature of itching hyperexcitability in eczematous dermatitis.

Significant contributions to the physiology of sebaceous glands were made by H. Tanaka, University of Niigata. Among other achievements, by use of radioisotopes he demonstrated synthesis of phospholipids by skin tissue, fatty acid synthesis in sebaceous gland conglomerates of human axillary skin, and uptake of fatty acids into the sebaceous glands after parenteral injection of labeled material in vivo. He discovered a remarkable relation in amounts of RNA and glycogen in sebaceous gland cells and found that atrophy develops in these glands when dietary fat consists of oleic acid only.

On the whole, my impression of dermatological research in Japan was this: The Japanese investigators follow closely the world literature and are well informed about progress abroad. With genuine devotion, great ambition, perseverance, and fantastic diligence, they take a major share in this progress. Much of their work, as just described, in first class. Some investigators, however, sometimes test too many methods at once, and with many conflicting data on their hands, they are in danger of losing the leading idea. I also sometimes wished that, just like our own men, they would be more critical and discriminating of what they read in Western publications and thereby save time and effort.

The majority of the hospitals and laboratories in Japan are old. Modern equipment is difficult to get. Financial support of research is not easy to obtain. This is one more reason that their performance should be highly respected.

It was a great honor for me to have been invited to deliver the first Dohi Memorial Lecture in the Japanese Dermatological Society. I am forever indebted to my Japanese hosts, and particularly to Drs. Kitamura, Kobori, Dr. Y., and Miss Chicko Kuno, Drs. Miura, Sakurane, A. Takahashi, Y. Takahashi, Tanaka, Yamamoto, and Mrs. Yasuda for the unforgettable experience of having seen their beautiful country and for their gracious hospitality.

Section of Dermatology, Department of Medicine, The University of Chicago.

The VII International Congress on Leprology*

November, 1958, in Tokyo

The VII International Congress on Leprology was held in November, 1958, in Tokyo. It was originally scheduled for New Delhi, but rather involved diplomatic reasons compelled the government of India to withdraw its invitation. Our Japanese colleagues, under the auspices of the Japanese Leprosy Foundation and under the leadership of Prof. Dr. K. Kitamura and Dr. K. Hamano, extended an invitation to hold the Congress in Toyko and did a remarkable job organizing such a big undertaking with only three months' time for preparation.

Delegates from 41 nations attended the Congress, which was officially sponsored by the brother of Emperor Hirohito, His Imperial Highness, Prince Takamatsu.

The headquarters of the Congress was in the Sankai Kaikan Building, one of the finest conference sites one could wish for. Meetings took place in the International Conference Hall, modeled after the Security Council of the United Nations in New York. All papers and discussions were simultaneously translated into English, Spanish, Japanese, and French, and one was able to listen to the desired language with the help of earphones and a selector switch. Adjoining the Conference Hall a special post office, rooms for secretaries and translators, a travel bureau, and similar facilities made life most pleasant for the delegates. Speakers had to hand in their slides at least 24 hours in advance at a special desk. They were tested and trial-projected in a separate room. At the time of the meeting four projectors, each manned by a projectionist and all of them under the orders of a head projectionist, did an outstanding job. In addition to the main large screen for the projection of illustrations and tables, a smaller screen on the left side showed name and title of the paper being presented, while a screen on the right side was used for announcements.

As in all International Congresses on Leprology, Classification was the cause for the most heated discussions and marked disagreement. The two main types, lepromatous and tuberculoid, as accepted at the last International Congress, in Madrid, remained unchanged. So, also, did the indeterminate group and the borderline, or dimorphous, group. The Indian leprologists demanded the addition of a macular-anesthetic group because they felt that these cases, frequently encountered in their country, constitute a distinct clinical entity and cannot be classified as belonging to the tuberculoid type. They further wanted to have a special group created for neuritic lesions (polyneuritic or mononeuritic) and call this the neuritic group. The Latin-American leprologists opposed both proposed new groups because they felt that careful examination and observation would show that patients supposedly belonging to them can be included in one of the existing types or groups. Further studies with special emphasis on correlation of clinic and pathology were suggested and planned. This is a point where we dermatologists have a great advantage, being used to correlate clinic and pathology, and it was rather frustrating to listen to numerous excellent papers and discussions on the merits of this or the other classification without being shown a single clinical or histological picture. On account of the very marked disagreement, no decision was made at this Congress and this matter was left to the discretion of the individual leprologist.

My paper, "A Dermatologist's Report on Leprosy in California," discussing 135 cases diagnosed during the last 10 years, was profusely illustrated with clinical and corresponding histopathological pictures of the various types and groups of cases. I think it helped stress the value of presenting clinical and histopathological pictures in any discussion of leprosy, and I have the impression that this will be done to a greater extent at the next International Congress on Leprology, which is planned to be held in Argentina, in 1963.

As far as therapy is concerned, the sulfones still dominate, despite their numerous toxic effects and complications. Several new drugs were mentioned and discussed. One of them was a thiourea compound—4 butoxy-4' dimethyl amino diphenyl thiourea—which supposedly has the advantage of low toxicity and seems therapeutically useful in cases in which sulfone therapy is not well tolerated. It has to be administered daily in doses of 25 to 40 mg. per kilogram of body weight and is rather expensive; therefore, at present it is unsuitable for mass treatment. Another most interesting new drug is a derivative of ethyl mercaptan (diethyldithioliso phthalate) called ETIP, or Etisul. It seems to be most effective, and one of the most interesting features of this preparation is that it is given by inunction, reminding the older ones of us of the classic mercurial inunction treatment of syphilis. Antigen Marianum, which received some publicity during the last few years, has

* Special Report.

been disappointing and its use in the treatment of leprosy was not recommended. Great emphasis was placed on reconstructive surgery and the necessity of making it available to all patients. In that respect, excellent results were demonstrated by our Japanese colleagues in the various leprosaria.

It was interesting and gratifying for me to see that the lepromin test was given added importance. However, it was recommended that rigid standardization in its production, as well as in the interpretation of the reaction, be carried out. No agreement was reached regarding the value of BCG vaccination to convert a lepromin-negative person to a positive one; however, it was suggested that lepromin-negative contacts should be given BCG vaccination and that young children may be vaccinated without a preliminary lepromin test. In the Section on Bacteriology and Pathology (Chairman, Dr. J. H. Hanks, U. S. A.), tissue culture (Dr. C. C. Shepard, U. S. A.), electronmicroscopy (Dr. Mitsugu Nishiura, Japan), and inoculation experiments (Dr. D. H. Binford, U. S. A.) (golden hamster) were some of the subjects discussed.

Of special interest to us in the United States was a statement read by Dr. George Fite in which the need for a revitalization of the Public Health Service Hospital in Carville was acknowledged and plans discussed to make it a research center for leprosy in the United States, where all the aspects of the disease will be considered. An appropriation of $90,000 by Congress, earmarked for this purpose in 1958, was a step in the right direction.

Another outstanding representative of the United States Public Health Service Hospital in Carville was Sister Hilary Ross, who was, as always, indefatigable and took a prominent part in all the scientific activities of the Congress.

One of the highlights of the Congress was the fact that the great old master of leprology, Dr. K. Mitsuda, attended and was most gracious to all the vistors.

Delegates were invited to visit the National Leprosy Research Institute, where the character of the research carried out is impressive and the equipment, including electronic microscopes excellent. The National Leprosarium, Tama Zensho-en, situated adjacent to the Research Institute, has a capacity of 1,470 patients and is a city in itself. Its director is Dr. Yashinobu Hayashi. Patients live in bungalows, and there are excellent facilities for physical therapy and reconstructive surgery. These institutions are approximately 30 miles out of Tokyo. I was able to visit two other leprosaria located in the beautiful Hakone National Park. One was the Suruga National Leprosarium, with approximately 460 patients, most of them very advanced cases. It was originally intended only for Japanese soldiers suffering from leprosy but now admits any patient with this disease. We received a most impressive welcome, all the patients turning out led by a music band and an honor guard formed by soldiers. From there we went to the Koyama Leprosarium, which is run by the Missionary Sisters of Christ the King from Canada and is certainly a most impressive place. It has 105 beds and excellent facilities. It was especially gratifying to see and hear that many of its best features, such as a most modern surgery, were built and are maintained with donations from the United States.

Extensive social events were held in honor of the delegates, such as a reception by Prince and Princess Takamatsu at the Korin Palace, a reception by the Governor of Tokyo at the Kiyosumi Garden, a theater performance at the Takarazuka Theater as guests of the Minister of Health, and a party given by our Japanese colleagues for the attending dermatologists, combining Kodachrome presentation and discussion of unusual cases with a most lavish and elaborate dinner.

The meeting was extremely well organized, and many features would be worth copying at the next International Congress on Dermatology to be held in the United States in 1962.

PAUL FASAL, M.D.
San Rafael

Meeting of the International Society for Human and Animal Mycology*

The International Society for Human and Animal Mycology held the first meeting Sept. 5 to 8, 1958, in conjunction with the Sixth International Congress for Tropical Medicine and Malaria in the recently built and magnificently equipped Institute for Tropical Diseases, Lisbon. About 100 persons attended the sessions, which consisted of two business and six scientific meetings.

The main topics were as follows: clinical and epidemiological aspect of mycoses was reported by C. S. Lacaz of San Paolo; Vanbreuseghem related his findings on African histoplasmosis, and Drouhet, on the mycological aspects of West African histoplasmosis, particularly on the effect of amphotericin B on the disease. Leite Salazar gave an account of the epidemiology of superficial mycoses in Angola and Mozambique. P. Abbot and P. Destombes discussed the epidemiology of mycetomas, the latter stressing particularly osseous involvement.

The second session dealt with the ecology of fungi, which was introduced in a scholarly essay by Dr. C. W. Emmons. G. C. Ainsworth discussed the oral flora, stressing the mouth as a potential reservoir for pathogenic fungi. R. O. Egeberg, A. Elconin, and C. M. Chahoon presented the result of four-year studies in the southwest Joachim Valley of California. According to their statement, the rate of recovery of the fungus varies with the specific location from which the soil sample is taken. The highest recovery rate is on the surface three or four weeks after the end of the rainy season, being most consistent in the walls of the animal burrows and being lowest in the soil obtained from the surface toward the end of the dry season, when the incidence of the disease is the highest. L. I. Lurie reported his findings that South African histoplasmin sensitivity is mainly found where yellow podzolic soil is found. E. B. Durie recovered from Australian soil samples several pathogenic fungi, also a new species: Trichophyton terrestre. Van Uden of Lisbon drew the attention to the intestinal yeast flora of man and animals and stressed particularly that, since Cryptococcus neoformans has been isolatd by him from the fecal contents of a healthy horse, equines may sometimes also contribute to the dispersal of this pathogen.

Submitted for publication Dec. 12, 1958.

* Special Report.

The third scientific session dealt with the biochemistry and physiology of pathogenic fungi. G. Segretein, of the Pasteur Institute of Paris, referred to his previous studies on vitamin growth requirement of certain pathogenic fungi. His studies dealt with cell respiratory enzymes of the genus Candida. The main part of this presentation dealt with various factors which are responsible for the transformation of the mycelial into the yeast phase of certain pathogenic fungi. H. Seeliger, C. Lacaz, and C. M. S. Ulson investigated agglutination and precipitation reactions for the identification of black yeast-like fungi. F. Mariat presented his biochemical investigation for the identification of Nocardia and Streptomyces which have been isolated from mycetomas. Aldo Castellani presented mycological methods whereby it is possible to determine copper-reducing and non-copper-reducing compounds. M. P. Miguens gave evidence on the basis of his auxonographic studies that Trichophyton quinckeanum can be easily differentiated from Trichophyton mentagrophytes and Trichophyton rubrum.

The "Free Communication" included a large number of challenging papers. J. Schwartz emphasized the cultural similarities between Histoplasma capsulatum and Histoplasma duboisii but referred to the characteristic giant forms of H. duboisii. B. Ettig studied the influence of soil on pathogenic fungi and found that dermatophytes grow on non-sterilized field soil, garden mould, and compost, whereas it was not possible to grow these fungi on sterilized soils.

K. Ishida isolated C. neoformans from pulmonary granuloma of a cat and also from pigeon droppings and from droppings of the Japanese skylark (Alauda arvensis japonica). J. Esteves and H. Neves presented a study proving that parasitized hair is more suitable to produce cutaneous experimental infections on human beings than with cultures of Trichophyton violaceum.

Paldrock gave an account of the contributions to mycology made by Scandinavian investigators. He also recommended his classification which combines both botanical and clinical points of view. R. R. Brygoo presented his findings on the incidence of chromoblastomycosis and mycetomas on Madagascar, and Yamato communicated the first case of histoplasmosis in Japan. J. R. Vieore described a case of onychomycosis caused by Aureobasidium pullulans. J. Gentles of Glasgow gave a

challenging account of a successful treatment of dermatomycoses with a new antibiotic, griseofulvin. His results indicate that the drug is rapidly absorbed and that keratin formed during treatment is resistant to the invasion of ringworm fungi. His report dealt only with results obtained on guinea pigs, but the drug has become recently available for humans by the Glaxo Laboratories, Ltd., London, and by Johnson & Johnson, and Schering Corporation in the United States. The recommended dose is one gm. daily for not more than 20 days. Trichophyton purpureum infections are particularly responsive to this treatment. Memersheimer proposed a method for the testing of orally administered antifungal remedies. The procedure consists in sensitizing guinea pigs with chlordinitrobenzol and a subsequent infection with either Candida albicans or T. mentagrophytes. Whereas, the skin lesions disappear in two to three weeks after the infection, the presence of these fungi persists in the lymph nodes for several weeks, sometimes for months.

This is a condensed report of the scientific part of the meeting. In addition to these, several challenging and stimulating papers have been presented which can be read in the official transactions of the Congress.

Those who attended the Congress not only enriched themselves with considerable valuable new information but enjoyed a rare opportunity of international conviviality and, particularly, of unique Portugese hospitality.

FREDERICK REISS, M.D.
870 5th Ave.
New York 21

The Epidermal Biopsy

Its Indications and Technique

ROBERT P. ARTHUR, M.D., and WALTER B. SHELLEY, M.D., Philadelphia

For a number of years we have employed a razor shaving technique for securing superficial skin biopsy specimens, both in clinical practice and in research. The success and simplicity of this procedure prompt us to record our observations for those who may be unfamiliar with such an approach. Furthermore, recent papers on the cutaneous biopsy fail to mention the epidermal biopsy.[1-3]

In our experience the epidermal biopsy is most useful clinically in the study of superficial lesions of the face, hands, or feet. In these critical areas the significant primary lesion can often be removed as a superficial shaving without the hazard of scarring. The need for a histologic study of areas in which healing may be delayed, such as the lower leg or intertriginous sites, is also a prime indication for the epidermal biopsy. Thus, we have employed this technique with success on superficial fungating masses in the groin, as well as in patients with coagulation defects. We have found that the biopsy-resistant patient, child and adult alike, can be persuaded to submit to such a procedure, which may be described euphemistically as " a scraping for laboratory study." By definition the epidermal biopsy is limited in usefulness to the study of those processes which affect the outermost layers of the skin. Yet daily practice reveals a significant number of dermatoses primarily situated in the epidermis or papillary layer of the corium. Thus, we have employed the technique with profit in the diagnostic study of (1) eczematous reactions, e. g., dysidrosis, contact dermatitis, scabies; (2) psoriasis, lichen planus, keratosis follicularis; (3) vesicular reactions, e. g., miliaria, dermatitis herpetiformis; (4) scabies, tinea corporis; (5) minor growths, or masses, e. g., nevi, seborrheic keratoses, epitheliomas, sarcoidosis, granuloma annulare, lichen nitidus.

In clinical research the epidermal biopsy technique permits one to secure almost innumerable specimens with minimal discomfort and cosmetic disturbance. We have secured as many as 20 epidermal biopsies from a single patient at one time in our studies on epidermal innervation. In

Submitted for publication Dec. 22, 1958.

Veterans Administration Hospital and the Department of Dermatology, University of Pennsylvania School of Medicine.

Fig. 1.—Technique of obtaining razor epidermal biopsy. Skin is kept under tension as psoriatic lesion is gently shaved. Note thin, epidermal specimen lying on razor.

Fig. 2.—Low-power view of histology of tissue obtained in Figure 1. Note that specimen is essentially epidermal. Reduced about 35% from mag. × 30.

analyzing the histologic effects of therapy or simply the course of the disease, serial razor biopsies may be of considerable value to any investigator. With experience, specimens can be obtained which are essentially epidermis, again affording the observer an opportunity to study the chemistry or physiology of the major divisions of the skin. Such a technique has been employed by Buhmann,[4] for example, in Warburg studies of the epidermal metabolism. Actually, epidermal specimens obtained in this manner may be far larger than any which might be secured by scalpel biopsy technique. In addition a further advantage in chemical work accrues from the fact that epidermal biopsies may be performed without the injection of a local anesthetic. Finally, it should be noted that such shaving biopsies may be of value in a variety of studies ranging from tissue transplants to tissue culture.

The actual clinical procedure is a simple one. First, hunt for the most definitive primary lesion. This may be a single micropapule or a rather large plaque. Almost any size epidermal specimen can be removed, ranging from a lesion less than a millimeter in diameter to one several centimeters in width and length. When coupled with serial sectioning, the larger specimens provide the pathologist with an unrivaled view of the epidermal changes. The site to be biopsied is infiltrated with a local anesthetic (procaine, tripelennamine [Pyribenzamine]) or just saline in the allergic person. Actually, the specimen can be lifted without injection anesthesia in the more stoic patient. The only instrument necessary is the razor edge. We have found half a Gilette Blue Blade to be ideal. It has sufficient thickness to remain under close control. Thinner, as well as thicker, single-edge blades have not proved as satisfactory. The blade may be held in the hand (Fig. 1) or in a needle holder. For small biopsies, one may cover the cutting edge with Scotch Tape except for the desired width at the very tip.

The skin is held taut as the razor blade is used to shave off a very superficial specimen. A fresh sharp benzalkonium (Zephiran)-sterilized blade is used for each biopsy. A gentle sawing motion may be used. A little experience is needed to judge the proper depth for cutting. The tendency is to go too deep, although in acanthotic lesions considerably more depth is desirable. The specimen slides up over the top of the blade as a thin bloodless gray sheath (Fig. 1). The corium presents numerous capillary bleeding points which can be stopped by a pressure dressing, absorbable

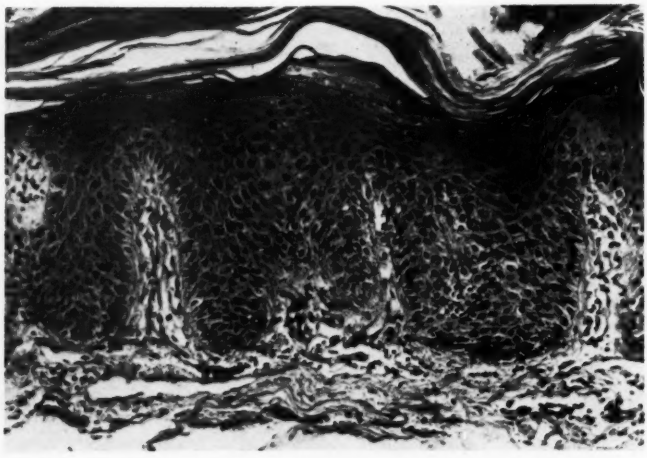


Fig. 3.—Medium-power view of same epidermal biopsy specimen of psoriasis. Tissue is adequate for histopathologic purpose. Reduced about 35% from mag. × 225.

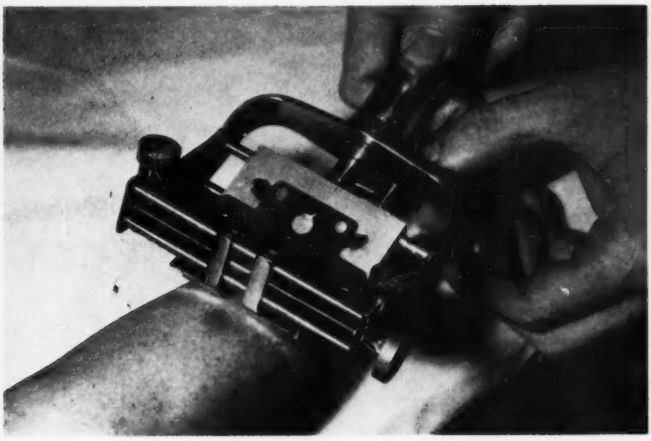


Fig. 4.—Brown electrodermatome for obtaining large strips of epidermis of uniform thickness. Its usefulness is greatest in clinical research studies requiring large amounts of tissue.

gelatin sponge (Gelfoam), or very light electrodesiccation. Once hemostasis is achieved, the area is left open to form a healthy crust. After a variable time this crust falls off, leaving a depigmented hyperemic zone which gradually is restored to normal skin color and appearance. With proper depth there is absence of scarring.

The specimen, still on the razor, is placed in formalin or appropriate fixative with instructions for the pathologist regarding orientation for sectioning. Within an hour the specimen can be imbedded and cut.

In addition to the manual specimens for clinical study, we have also obtained for research purposes very satisfactory large sheets of epidermis with use of the Brown electrodermatome* (Fig. 4). This motor-driven unit will permit one to secure rather unlimited sheets of superficial skin of any predetermined thickness. Cutting is achieved by a special oscillating razor-edge blade which may be set at any desired level for depth. The width may be adjusted from 1 to 8 cm. After anesthesia is achieved, a thin film of sterile mineral oil or powder should be spread over the skin to facilitate operation of the dermatome. It is important that the skin be kept taut at all times during the cutting. The instrument is pressed down firmly against the skin, and it is moved slowly and steadily forward until the end of the cut is reached. At that point tilt the front of the unit up to cut off the skin.

*Zimmer Manufacturing Company, Warsaw, Ind.

Summary

A simple rapid razor technique is described for obtaining epidermal biopsies. The procedure leaves no scar, requires no sutures, and is followed by rapid healing. It is recommended that it be employed to obtain histopathologic data in those instances in which a full-thickness skin biopsy would be unnecessary or be medically or cosmetically undesirable.

Duhring Laboratories, Department of Dermatology, University of Pennsylvania (4) (Dr. Shelley).

REFERENCES

1. Goldman, L., and Preston, R. H.: Special Small Knives for Minor Dermatologic Surgery, A. M. A. Arch. Dermat. 78:640, 1958.

2. Caro, M. R.: Diagnostic Pitfalls of Dermal Pathology, A. M. A. Arch. Dermat. & Syph. 67: 18, 1953.

3. Urbach, F., and Shelley, W. B.: A Rapid and Simple Method for Obtaining Punch Biopsies Without Anesthesia, J. Invest. Dermat. 17:131, 1951.

4. Buhmann, A.: Atmung und glykolyse in normaler und pathologisch veränderter Haut, insbesondere mit Hinblick auf Psoriasis, Biochem. Ztschr. 287:145-152, 1936.

The Prismatic Binocular Microscope Adapted for Dermatologic Use

H. C. GOLDBERG, M.D., Plainfield, N. J., and J. KINDLER, M.D., East Orange, N. J.

The illustrations show an adaption of a prismatic binocular microscope which has proven itself invaluable in our practice. Head loupes, hand magnifiers, shop and pocket microscopes, and stereobinocular microscopes have been described[1] which have been inadequate or cumbersome resulting in disuse and unpopularity of these instruments. Recent first hand observation of a stereoscopic binocular microscope suggested extremely simple changes which makes it possible to use this fine instrument for dermatologic purposes.

Submitted for publication March 5, 1959.

The illustration (Fig. 1) shows such a Kern prismatic binocular microscope as it is ordinarily used. The body of the microscope is on a stand ready for observation of material placed on this stand. Various light attachments and arrangements are available for this. By removing the stand and

Fig. 1.—Kern prismatic binocular microscope as it is ordinarily used.

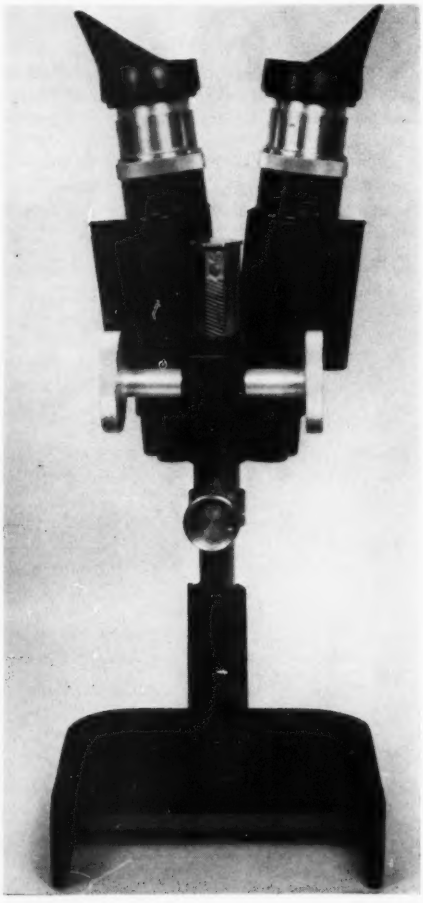
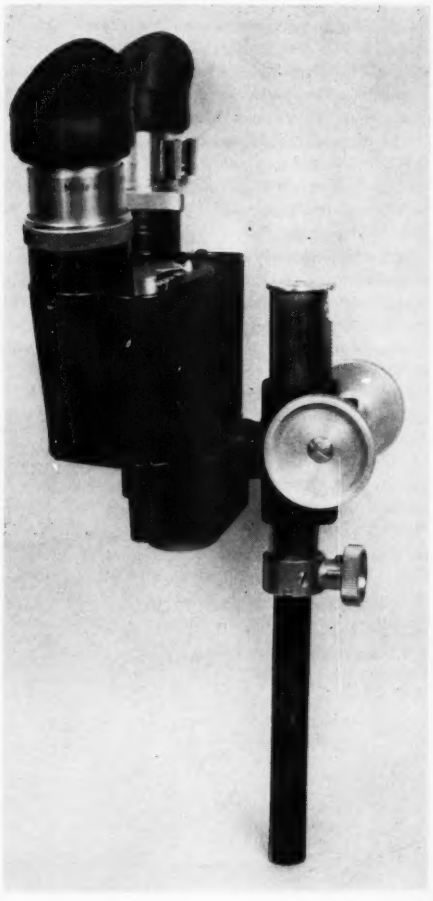


Fig. 2.—Adaptation for dermatologic use.



inserting a (painted) wooden ½ in. dowel 6¼ in. long, the instrument becomes an easily hand-held and supported microscope, which rests on its newly created unipod on whatever part of the body the examiner wishes to inspect closely.

The unipod is placed at rest on the skin about ½ in from the area to be placed in focus for examination. An allergy vial rubber cap fits easily over the end of the dowel and is comfortable for contact with the patient. Various magnifications are available and these are easily interchanged, but I have found the lowest-power lens to give a × 10 magnification, which is excellent, without demanding a critical focus, which is difficult to obtain and/or to maintain.

Since the usual adjustable office examining lamps are readily at hand, they provide an adequate source of light without encumbering the instrument with attachments.

When the microscope is held on the patient, excellent magnification of various skin areas is readily obtained with ease and comfort for both patient and doctor. Figure 2 shows the focusing-rack control. The rubber eyepiece hoods are a necessity. They shield the eyes from the floodlight of the office examining lamp used for illumination of the skin surface.

The improvement in vision is remarkable and clinches many doubtful and unsettled problems. It literally opens a new worl[1] for the clinician and requires reevaluation of our usual dermatologic impressions of many skin lesions.

The instrument illustrated is obtainable from August Waeldin, Inc., 10 Maiden Lane, New York 38.

I wish to acknowledge the courtesy of Mr. Townsend Oliver in helping me work out this adaptation.

7 Watchlung Ave. (Dr. Goldberg).

REFERENCE

1. Goldman, L.: Clinical Studies in Microscopy of the Skin at Moderate Magnification, A. M. A. Arch. Dermat. 75:345-360 (March) 1957.

A Bland Bath

ELMER R. GROSS, M.D., Wilmington, Del.

The role that the bath plays in the dermatologic therapeutic armamentarium is well recognized. The virtues of colloids, oils, and many other bath additives have been extolled, and rightly so.

For the past 10 years I have routinely employed an inexpensive water softener,[1] a nonirritating, completely soluble, granulated powder readily available through grocery stores. This powder, sodium hexametaphosphate,* is conducive to restoring the protective acid mantle of the skin and is indicated wherever and whenever a bath is feasible in dermatologic practice.

In a routine bath, sodium hexametaphosphate is readily miscible with soap, does not precipitate colloids in any additives, and improves the efficiency of soapless detergents. As a sole agent, used in the bath in the treatment of dermatoses and inflamed skin, this conditioner imparts a very soft, silky feel to the water. For the ordinary tub, patients are advised to draw a lukewarm bath and to the water add 5 to 6 rounded tablespoons (about 75 to 90 ml.) of the powder, or enough to make the water feel very slippery. For extremely dry skins and for bathing in cold weather it is well to use a combination of sodium hexametaphosphate and a sulfonated oil,† also very soothing to the skin; in this instance only 4 tablespoons (60 ml.) of the conditioner would be advocated.

Medical Arts Building (1).

REFERENCE

1. Gross, E. R.: Care of the Dentist's Hands, J. Am. Dent. A. 40:452-454 (April) 1950.

Submitted for publication Dec. 26, 1958.

* Calgon, Calgon Co., a division of Hagen Chemicals & Controls, Inc., Pittsburgh (not to be confused with Calgonite, its alkaline counterpart).

† Bathovel, Torch Laboratories, Philadelphia.

ANNOUNCEMENT

Chicago Dermatological Society Annual Essay Contest.—The Chicago Dermatological Society is offering an annual cash prize of $500 for the best essay, not previously published, on some phase of dermatology or in the fundamental sciences relative to a dermatologic problem. It is the purpose of this contest especially to stimulate young physicians and other young scientists in research study on the structure, functions, and diseases of the skin.

Competition is open to members and accredited guests of the Chicago Dermatological Society, and all those scientists working within the Middle Western States who are sponsored (in writing) by a member.

Three copies of each manuscript, together with illustrations, charts, and tables are to be submitted to the Secretary of the Chicago Dermatological Society not later than Nov. 18, 1959.

The essays are to be judged on the following considerations: (1) originality of ideas and findings; (2) potential importance of the work; (3) clarity of presentation.

This contest is intended as an annual one, but, if in any year, at the discretion of the committee, no paper worthy of a prize is offered, the award may be omitted.

The results of this contest will be announced at the meeting of the Society on March 16, 1960.

Further information regarding this essay contest may be obtained by writing to the Secretary of the Chicago Dermatological Society, Frederick J. Szymanski, M.D., 55 E. Washington St., Chicago (2).

The New, Newer, and Newest

Like spring in Oklahoma, societies are busting out all over: Frederick Reiss is busy organizing a United States chapter of an International Organization on Tropical Dermatology.—A new Radium Society for Dermatologists has elected John Lamb, President, Robert Morgan, Vice-President, and Phyllis Jones, Secretary.—The Pacific Dermatological Society has heard the suggestion that it function as a regional Academy, meeting in cooperation with the larger organization, which is somewhat "unwieldy."—And information has it that things are beginning to shape up for the International Congress in 1962. A substantial grant has been obtained from the National Institutes of Health, and contributions have been received from national groups, such as the American Dermatological Association, the Academy of Dermatology, the Society for Investigative Dermatology, and various local organizations. The famed Philadelphia Symphony Orchestra has been engaged for one of the evenings.

Walter C. Lobitz Jr. has been appointed Professor and Head of the Division of Dermatology at the University of Oregon Medical School.

Anthony Cipollaro was honored by the New York City Cancer Committee and awarded a bronze medal from the American Cancer Society for his services as Chairman of the Committee on Education of the New York Chapter.

A Husik Medical Scholarship Fund has been established in the University of Pennsylvania Medical School of Medicine. Behind that announcement in the University of Pennsylvania Gazette for January, 1959, is an account of the amazing life story of dermatologist Dr. Maurice Husik, of New York City, who became a physician at the age of 42 after having been a professional dancer, actor, sculptor's model, school teacher, linguist, soldier, foreign relief administrator, and consular officer. It was in medicine that he found the "peace of conscience," and the scholarship was established by him as evidence of his high regard for a former teacher, Dr. R. Tait McKenzie.

In Florida, a bill to prohibit the tatooing of girls under 18 has been referred to the public amusements committee of the Florida House of Representatives.

In Newcastle, the British Medical Association was told that a young physician can make more money delivering Christmas mail or working as an apprentice cook in a hospital than by joining the staff of a goverment hospital—and

In the United States the possibility that one day the young physician may find himself in the same boat it there are continued both the present plague of biased antidoctor articles in some of the popular press and the many vicious malpractice suits for fantastic sums of money. Be shocked out of your sensibilities by the opening paragraphs of Milton Silverman's concluding article on "Medicine's Legal Nightmare" in the *Saturday Evening Post*, April 25, 1959. It tells a story of unbelievable ingratitude on the part of a family whose lives had literally been saved by conscientious and skilled physicians. It is about time we began to strike back instead of effacing ourselves because of the occasional justifiable suit.

Harvey Blank addressed the Illinois State Medical Society May 21 on "Systemic Therapy of Superficial Fungus Infections." Marcus Caro, Allan Lorincz, William Slinger, and Hilliard Shair also took part in the program.

The Arkansas Dermatological Association, which met in Fort Smith and was addressed by Harold Perry on the subject of drug eruptions, in April, elected Calvin Dillaha, President, and Lawrence Zell, Secretary.

Leslie Smith participates in the Oregon Cancer Conference July 16.

The new officers of the Southwestern Dermatological Society are Earle Pace, Santa Fe, President, George Waldriff, Albuquerque, Vice-President, and Henry Garret, El Paso, Secretary.

A well-known colleague's prescription for the teen-ager with acne, according to *Scope Weekly* of April 15, is to "give them lots of affection." That's what the man said!

H. R.

Society Transactions

BRONX DERMATOLOGICAL SOCIETY

Arthur B. Hyman, M.D., President
Henry Silver, M.D., Secretary
Morris Leider, M.D., Editor

Oct. 16, 1958

Diagnosis: Cutaneous Leishmaniasis (Treated with Dihydrostreptomycin). Presented by Dr. Laurence L. Palitz.

A 62-year-old woman came to this country four years ago from central Italy where she was born. Eighteen months ago she first noted on her nose a small "pimple" which "never came to a head." This lesion was removed by a dermatologist, and one diagnosis was "possible histoplasmosis" because histopathology was compatible and because histoplasmin tests were positive. The patient was first seen by me in April, 1958, at which time she presented a large ill-defined, raised, verrucous plaque covering the entire top of the nose. Part of the lesion was covered with a brownish-yellow adherent crust. Biopsy at this time revealed a granulomatous reaction with a dense cellular infiltrate throughout the entire cutis. The infiltrate was made up of lymphocytes, plasma cells, and large mononuclear cells, containing closely packed organisms which were identified as Leishmania tropica.

Throughout the course of the disease the patient has noticed transient plaque-like indurations under both eyes, which usually appear in the morning and slowly improve during the day.

Treatment has up to recently been of no avail. Stibophen (Fuadin) injections, quinacrine (Atabrine) and chloroquine (Aralen) by mouth; quinacrine and chloroquine injections into the lesions; x-ray therapy, and carbon dioxide cryotherapy were all tried with little success. Last week the patient was started on large doses of dihydrostreptomycin (2 gm. every day for five days) by intramuscular injection. The improvement has been dramatic.

Discussion

Dr. Mabel G. Silverberg: I have personally treated only one patient with this condition and in my patient the lesion, being more nearly classical, did not resemble the present one.

The present lesion looks very much like lupus vulgaris and, although leishmaniasis, sarcoid and tuberculosis of the skin must be thought of clinically, a differential diagnosis is usually possible microscopically. Since the causative organism was found in this case microscopically, it is a case of leishmaniasis, and it is good to have seen it.

Dr. Laurence L. Palitz: May I emphasize several points about this case? First, it responded dramatically to dihydrostreptomycin after failure to respond to agents and measures traditionally used in this condition. Second, recent reports suggest that small doses of steroids are helpful adjuncts, and, therefore, this patient was given methyl prednisolone (Medrol), 10 mg. daily, additionally, which may have contributed to the rapid improvement. Third, as nearly as I can estimate, the incubation period in this case is about three and one-half years, which is unusually long. The literature gives several months to one and one-half years as the range of incubation periods, but Dr. Jessner tells me that he too has observed cases with much longer incubation periods.

Diagnosis: Behcet's Syndrome (Aphthosis). Presented by Dr. Helen O. Curth.

Following high fever in 1940, the patient, then 12 years of age (now 30), developed ulcerations in the mouth and throat and two weeks later ulcerations on the skin. Since that time he has constantly suffered from recurrent lesions of the same sort. Most of the oral, cutaneous, and genital ulcerations have left scars. In 1948 he was admitted to the Presbyterian Hospital, where bacitracin was administered intravenously. He underwent a plastic operation of the oral cavity several years ago. He occasionally has what appears to be esophageal lesions.

Upon examination now the patient is unable to open his mouth widely. There are multiple ulcerations on the tonsils and buccal mucosa, which are covered with a grayish exudate and surrounded by red halos. The lower and upper lips show multiple erosions. The chest, back, and extremities are covered with numerous confluent scars. Between these scars there are some active lesions showing either central pustules surrounded by inflamed skin

Submitted for publication Nov. 25, 1958.

or ulcerated lesions covered with a gray adherent slough.

Extensive blood studies including bleeding time, tourniquet tests, coagulation time, heparin clotting times, clot retraction, prothrombin time, serum prothrombin time, platelet count, zinc sulfate turbidity, cryoglobulin search, and electrophoresis of serum were all within normal limits.

Bacteriologic studies of specimens taken from lesions on lips, tonsils, and scrotum revealed streptococci that were all bacitracin-sensitive.

Biopsy specimens of two lesions from the skin were read by Dr. G. F. Machacek as a furuncle in one and as perifolliculitis in the other.

Treatment with 10 cc. of γ-globulin every two weeks is thought by the patient to be more controlling than anything else ever prescribed for him.

Discussion

DR. CONRAD STRITZLER: I have repeated Dr. Curth's studies on coagulation defects in two patients with Behcet's syndrome, and thus far all studies have yielded normal findings.

DR. ABRAHAM J. ORFUSS: I should like to ask Dr. Curth to discuss the reasons for treating this patient with γ-globulin injections despite normal blood and serum findings.

DR. VICTOR H. WITTEN: I would like to ask whether the lesions which we see at this time are part of Behcet's syndrome. The numerous round-to-oval scars, the majority of which are soft with a somewhat protruding center and slight dimpling, resemble more the scarring which follows smallpox vaccination rather than that which follows furunculosis or folliculitis. Is it not possible that these lesions may be of virus etiology but are not a part of the syndrome here referred to as aphthosis?

DR. HELEN O. CURTH: Aphthosis may affect several organs besides the oral cavity, genitals, and eyes. Recently, the involvement of the central nervous system has been widely discussed. I believe that in the patient presented tonight the skin is the organ most deeply affected. Other patients suffering from Behcet's syndrome occasionally have cutaneous lesions similar to what is seen here. Lever (discussion to Fromer, J.: A. M. A. ARCH. DERMAT. 77:459 [April] 1958) mentioned another instance of Behcet's syndrome with generalized cutaneous lesions of this type. The present patient has in addition to the cutaneous lesions recurrent oral and genital ulcerations typical of aphthosis. The scars are the end result of ulcerative lesions. They are stretched because the patient is a very thin person. The affected organ acquires a high degree of local sensitization to whatever factor or agent is responsible so that new lesions develop among scars from previous lesions. This also takes place in the oral cavity and on the genitals. To the question of why γ-globulin was employed, the answer is on experimental grounds of a reasonable and hopeful thing to do in spite of normal serum partition.

Diagnosis: Mycosis Fungoides. Presented by DR. ABRAHAM J. ORFUSS.

A white man, aged 66, is presented with a history of a pruritic, persistent, slowly progressive eruption said to have been present for about seven to nine years.

Examination reveals symmetrically scattered, grouped and discrete, fleshy papules and nodules on the trunk, extremities, back, abdomen, and buttocks. Shotty nodes are palpable in the groin. The liver and spleen are not palpable.

Laboratory studies were negative with respect to examination of blood, urine, x-ray of the chest, and bone marrow.

Biopsy interpreted by Dr. Charles F. Sims was as follows: The upper corium presents a perivascular and diffuse cellular reaction which is composed of a pleomorphic infiltrate. There are many histiocytes, reticulum cells, and polymorphonuclear leucocytes; some red blood cells, and an occasional cell in mitosis. The vessels throughout are dilated, and their walls are edematous. The epidermis is irregularly acanthotic but otherwise not noteworthy. The diagnosis is mycosis fungoides.

The patient is, at present, receiving generalized teleroentgentherapy. One such treatment of 50 r has been given with factors of 50 kv. and 40 ma. The HVL of such radiation is 2 mm. of water and the TSD is 2 meters.

Diagnosis: Lymphoblastoma of the Skin (Response to Teleroentgen Radiation). Presented by DR. EARLE W. BRAUER and DR. ABRAHAM J. ORFUSS.

A 33-year-old white man first came under observation in April, 1957. At this time the patient presented a generalized, slightly pruritic, scaly, erythematous eruption, arranged in plaques with very little infiltration. The eruption was of six months' duration. Biopsy specimens from the right and left shoulders were taken, and a histopathologic diagnosis of lymphoblastoma was made.

A course of Fowler's solution was begun and discontinued after approximately six weeks because of symptoms of diarrhea. Then geographically shaped, infiltrated plaques appeared over the body. Two areas over the right shoulder and right upper lateral aspect of the back were given two treatments of 150 r each two weeks apart of conventional superificial roentgen radiation (HVL of 0.9 mm. Al). Significant involution of infiltrations at these sites was noted. Three weeks later, the patient was referred for teleroentgen radiation.

The technique of teleroentgen radiation employed was as follows: The entire anterior and posterior surfaces of the body (only eyes and genitalia shielded) were given 50 r every other day (three times weekly) for three weeks (nine treatments to each surface). The radiation was generated at 50 kv. and 40 ma. The TSD was 2 meters, and the HVL was 2 mm. of water. A total of 450 r was thus administered to each surface.

After four treatments the patient showed clinical resolution in all areas and symptomatic improvement. Upon completion of treatment a near asymptomatic status was achieved and is still maintained.

Discussion

DR. ABRAHAM J. ORFUSS: I am presenting the case of mycosis fungoides for two reasons, namely, to illustrate the rather uncommon papular form of this disease and to give Dr. Brauer a chance to discuss the use of teleroentgen therapy in mycosis fungoides.

DR. ARTHUR B. HYMAN: Do you know of cases that responded to this kind of ray but did not respond to cathode ray and vice versa?

DR. VICTOR H. WITTEN: If I may answer Dr. Hyman's questions, I recall a 40-year-old woman from private practice who received a course of teleroentgen therapy, as outlined by Dr. Brauer, at the New York Skin and Cancer Unit (450 r fractionated over a three-week period). The slight benefit which was derived from this therapy was of only short duration, and approximately four months later arrangements were made for this patient to receive the cathode-ray treatment under the care of Dr. Fromer in Boston. The response to a course of this radiation was more effective than the teleroentgen therapy in flattening the lesions and reducing the itching. A second course of cathode-ray therapy was given again in four months and a few additional treatments three months after that. I now hear that the patient is deteriorating. So, while cathode radiation seemed better than teleroentgen radiation, neither is good enough.

DR. EARLE W. BRAUER: For more than a year, we have been investigating whole-body radiation at a focal skin distance of 2 meters in the physical therapy section of the New York Skin and Cancer Unit. Our work is based on a report which appeared in the *Journal of Investigative Dermatology* (Shirren). The quality of the beam utilized is extremely soft and therefore its absorption is almost complete in the skin. This type of radiation is not to be confused with that being utilized by Dr. Fromer and his group in Massachusetts. The latter are using a cathode-ray apparatus which shoots electrons at the skin surface under highly controlled methods of limiting the depth penetration.

Thus far we have treated approximately 25 patients, and the results have been encouraging. Our material has been almost exclusively patients with lymphoblastomas. Unfortunately most patients remained in a remission for only 6 to 10 weeks. A gradual return of subjective and objective findings takes place with severity similar to that present before treatment. This method appears, however, to have some value. It is still under investigation. We are trying now to find a treatment schedule which will provide long-lasting benefits to the patient, perhaps by regular but widely spaced additional treatments after good remission has been obtained by an initial, relatively intensive course.

DR. JOHN GARB: I am compelled to rise amidst this discussion to recommend again the treatment of mycosis fungoides with antimonials. As we see tonight and have seen for many years, radiation therapy is not as yet a good lasting treatment for this condition. It helps a little and for a short time. Perhaps it will be developed to be better. But in the meantime antimonials have controlled some cases for periods of years, not weeks or months only. I have three cases under observation at present with 8- to 10-year remissions. I frequently wonder if x-ray therapy does not promote transition of mycosis fungoides into leukemia, Hodgkins' disease, reticulum-cell sarcoma, or other lymphoblastomas. I wonder too if antimonials should not be the drug of first choice in mycosis fungoides and only upon its failure should resort be made to radiation modalities, the new cytotoxic drugs, and steroids.

Case for Diagnosis: Solitary Lesion of Urticaria Pigmentosa? Presented by DR. JULIUS H. POLLOCK.

A boy of 13 months has a nodule on the lateral aspect of the ankle over the malleolous. The mother states that the lesion appeared two weeks after birth and has enlarged to its present size which is about 1×1½ in. in diameter. It is rough in surface, yellowish, and sharply defined. Stroking causes noticeable swelling. The mother states that rubbing results in "blisters."

The case is presented to elicit opinion on the plausibility of the diagnosis of urticaria pigmentosa. The parents are not willing to permit biopsy.

Discussion

DR. SAMUEL B. FRANK: In reference to the crusted portion of the lesion that is now present, I obtained the statement from the mother tonight that she produced it by stroking the lesion. She had seen this procedure done so frequently at the clinic that she wanted to try it herself.

I am one, among others who had the temerity to make the diagnosis of urticaria pigmentosa based on the clinical appearance of the lesion.

DR. ALFRED W. KOPF: Among the several cases of solitary lesions of urticaria pigmentosa seen in the oncology section of the Skin and Cancer Unit, there is one boy, age 2 years, whose mother upon questioning revealed that she herself has widespread urticaria pigmentosa of several years' duration involving mainly the trunk. To my knowledge this is the only case in which a child with a single lesion of urticaria pigmentosa had a parent with the generalized cutaneous form of the disease.

DR. ARUTHUR B. HYMAN: A biopsy would have to be performed before definitive diagnosis can be made. There are lesions other than urticaria pigmentosa in which rubbing may lead to the formation of a bulla. On clinical grounds one feature which, I think, is against the diagnosis is the thick and roughened verrucous surface. Lesions of the disease seldom show surface changes other than thinning of the epidermis which is then notably smooth.

Urticaria pigmentosa has been reported in twins.

Diagnosis: Histiocytosis X. Presented by DR. ANDREW G. FRANKS and DR. R. FLEISCHMAJER (by invitation).

Seven months ago, a 15-month-old infant developed an eruption on the scalp which spread to the ears, neck, body folds, palms, and soles. In its beginning and still to a large extent, the eruption resembled seborrheic dermatitis. Four months ago, the patient suddenly showed petechiae on the abdomen, cervical adenopathy and ran a fever (temperature of 100-103 F). At the same time the liver became palpable to an extent of 2 finger breadths below the costal margin and vegetating lesions appeared around the vulvoanal region. Since then the patient has had several more febrile episodes, the spleen too has become palpable, more adenopathy has appeared, and what looks like a xanthoma has developed on the left check.

Laboratory studies of significance are as follows: Cholesterol determination was 390 mg. % on one occasion and 560 on another. Serum chlorides were 97 mEq. per liter; sodium, 137, and potassium, 5.3. The stool showed occult blood on one occasion and was negative on another. Cultures from the ears grew Pseudomonas from one and Proteus from the other. Bone marrow showed a normal picture. X-ray examination reveals "lytic" lesions in the parieto-occipital regions. The ascending rami of the mandible on the left side are destroyed. More "lytic" process is seen in the pelvis. Heart, lungs, and mediastinum are normal.

Treatment to date has consisted of steroids (prednisone, 20 mg. daily), antibiotics (penicillin, chloramphenicol [Chloromycetin] and erythromycin), and iodochlorhydroxyquin (Vioform) and hydrocortisone ointment topically.

Discussion

DR. SAMUEL B. FRANK: I have had a patient with this condition under my care for the past nine months. At 14 months of age this child had what looked like impetiginized seborrheic dermatitis on the scalp and follicular, crusted lesions on the body. The general resemblence to the case shown tonight is striking to me. Dr. Hyman made the diagnosis from the microscopic features. The patient is now 23 months old and seems to be thriving on steroid therapy.

DR. MORRIS LEIDER: On the wards of Bellevue Hospital we have an adult in her late forties who has been under observation for several years for the condition now labeled histiocytosis X. At the beginning of her trouble and at present, when her trouble seems to be coming to a sad end, the cutaneous picture is again like that of the infant shown tonight. It seems as if the cutaneous concomitant of this reticuloendotheliosis is a cross between what looks like seborrheic dermatitis, keratosis follicularis, impetigo, and pyoderma vegetans.

DR. SAMUEL B. FRANK: Dr. Leider's remarks are most pertinent to my experience with the case I cited. It was because I had the opportunity of seeing the case he refers to that I was led to investigate and resolve my case properly. I can confirm that the cutaneous features of all cases we are noting here are remarkably similar.

DR. ARTHUR B. HYMAN: In spite of acceptance of the term histiocytosis X by most general pathologists, it is a pity that we dermatologists do not use the much preferable term introduced by Dr. Hermann Pinkus, namely, reticulogranuloma.

I would like to ask Dr. Fleischmajer to tell us about the transition of Hand-Schüller-Christian disease to eosinophilic granuloma.

DR. RAUL FLEISCHMAJER (by invitation): During the first stage of the disease, this child presented the characteristic manifestations of Letterer-Siwe disease, namely, high fever, lymphadenopathy, a papular, purpuric rash on the trunk, a seborrheic dermatitis-like eruption on the scalp, a granuloma in the vulva and enlargement of the liver. Roentgen examination revealed destructive lesions on the skull, pelvis and the 10th dorsal vertebra. Later, the spleen also became involved. At present, the acute stage of the disease has subsided, due to continuous treatment with corticosteroids and antibiotics, and the clinical picture in now closer to Hand-Schüller-Christian disease than to the Letterer-Siwe syndrome.

An unusual finding was the presence of hypercholesteremia. Moreover, lately the patient has developed a xanthoma on the left check. I feel

that the increase in blood cholesterol levels is probably secondary to the liver involvement where some cirrhotic changes may have taken place. There is some collateral circulation, and the adbomen is prominent.

A unifying concept under the title of histiocytosis X suggests that Letterer-Siwe disease, Hand-Schüller-Christian disease and eosinophilic granuloma are different expressions of the same pathologic disturbance. Letterer-Siwe disease represents the acute phase; Hand-Schüller-Christian disease, the chronic stage, and eosinophilic granuloma, the mild, monosymptomatic form of the process. The term eosinophilic granuloma should be restricted to those cases where the involvement is of one organ, such as bone, skin, or lung. When two or more organs are involved, e. g., eosinophilic granuloma of the skin and/or the pituitary region and/or bone, etc., the proper label in such instances would be Hand-Schüller-Christian disease. The term histiocytosis X, proposed by Lichtenstein, is based on histopathologic grounds, namely, the presence of histiocytes which is a common finding of the three stages or types of the disease. Xanthoma cells are usually found in Hand-Schüller-Christian disease, but they are rare in Letterer-Siwe disease and eosinophilic granuloma, while eosinophils, always present in eosinophilic granuloma, are not too frequently seen in Letterer-Siwe and Hand-Schüller-Christian disease.

Diagnosis: Hemangioendothelioma. Presented by Dr. Conrad Stritzler.

A 6-year-old boy is presented with a history of a growing, small nut-sized purplish tumor on the middle of his back since about May, 1958. It was removed four months ago by electrosurgery but rapidly recurred.

One month ago it appeared as a rounded, sessile, purplish tumor about 3 cm. in diameter. The summit was soft and blanched slightly on pressure, but the base was firm and distinctly infiltrated. The clinical diagnosis was hemangioma or possible pyogenic granuloma.

Wide excision was done. Following is the biopsy report by Dr. Arthur Hyman: "The epidermis is stretched. The cutis shows a mass of rather well-defined groups of large, light-staining cells with rather big nuclei and vacuolated cytoplasm. Within the groups there are many dilated vessels near the upper cutis lined by these cells. Some mitoses are seen. Inflammation is mild, and there are wide margins of normal tissue. The diagnosis is hemangioendothelioma."

This case is presented to elicit expressions of opinion as to prognosis.

Discussion

Dr. Hans H. Biberstein: Four years ago I saw a boy, then 5 years of age, with a pea-sized angiomatous lesion on the left shoulder which was said to have appeared two months previously. I excised it and received a histologic interpretation of pericytoma. Five months later keloid formation appeared. Three x-ray treatments (¾ skin unit each time) resulted in a pale, soft, flat scar. The parents, who were very cooperative persons, never notified me of any further trouble and I assume with confidence that there has been none.

Dr. Alfred W. Kopf: Although these tumors are capable of metatasis, most authorities agree that fatalities from hemangioendotheliomas are rare. The clinical picture may be that of an ordinary hemangioma, as was in the case here. The condition is commoner in childhood and carries with it a somewhat guarded prognosis.

Dr. Charles Wolf: Since hemangioendothelioma has connotation of potential malignancy, I would suggest, though the lesion has been satisfactorily removed by surgery, a course of deep x-ray therapy of about 3,000 r as a prophylactic measure.

Dr. Arthur B. Hyman: Three thousand roentgens cannot be given with impunity to an infant. While the sections showed rather frightening features in the form of cellular pleomorphism and several mitotic figures in the endothelium of poorly formed vessels, such things are not equivalent in meaning as the same things in adults. The sheer immaturity of infants sometimes produces pictures of histologic activity which in many cases do not represent current or future malignancy. Therefore in this case, especially in view of the adequate surgery and lack of recurrence today, I would advise nothing but hopeful watching.

Diagnosis: Melanotic Freckle (Hutchinson) with Malignant Melanoma. Presented by Dr. Victor H. Witten and Dr. Alfred W. Kopf.

A 73-year-old white man noted the appearance of a brown "freckle" on the right cheek about three years ago. Since then the lesion has gradually and continually enlarged but has maintained the same color. There is no history of a preceding nevus or trauma and the lesion has been entirely asymptomatic.

On the right cheek there is a 10×14 mm. slightly elevated plaque which has mottled pigmentation varying from tan to brown to black. The perimeter of the lesion is ill defined and very irregular in outline. There is a mild scaliness of the surface. No nodules are seen within the lesion. There is no palpable cervical lymphadenopathy.

A biopsy specimen was taken from an area which was deeply pigmented (black). Dr. Arthur B. Hyman reported as follows: "The epidermis

is thin, and shows extensive though poor formation of junction theques. These fuse with intradermal elements, which are mixed with inflammatory cells and pigment granules. There are quite a few nuclear varieties, and I found three mitotic figures. This melanotic freckle is early melanoma."

Discussion

DR. MABEL G. SILVERBERG: Formerly these lesions were kept under observation and unless they underwent a marked clinical change they were left alone. I doubt that results are much better now with early surgical interference since adjacent normal-appearing skin is probably also involved in the degenerative process.

DR. ARTHUR B. HYMAN: Granted that lesions of this type are of rather low-grade malignancy, they still may, and not rarely do, develop ulcerating and nodular lesions which are malignant melanomas. Therefore, they should be treated. However, mutilating surgery is not called for. Eradication, certainly in the premalignant stage, by desiccation and curettage is in my opinion safe and might even be used here. Local, not too wide, excision, is more heroic and, of course, good practice.

DR. ALFRED W. KOPF: This entity which was described in the 1890's has recently come in for more attention. There are two phases, the premalignant and the malignant. The former is characterized by three clinical features: (1) changeability of size and pattern, (2) irregularity of the perimeter, and (3) mottling of pigmentation. The precancerous phase usually starts as a "freckle" in later years and often on the face. It slowly enlarges as a plaque of uneven color (tan, brown, sepia black) and irregular outline. After many years (average 10), in about one-third of such cases reported, a frank malignant melanoma develops *within* the freckle. For reasons as yet unknown the prognosis is considerably more favorable for malignant melanomas arising within such freckles. These are the generalities and many exceptions concerning onset, localization, and cause exist. It is interesting to note that Miescher (Miescher, G., and Hunziker, A.: Zur Behandlung der Melanome, *Schweiz med. Wchnschr.* 88:203-208 [March] 1958) states that one-fourth of the patients he sees with malignant melanoma the malignancy took origin from melanotic freckles.

DR. CHARLES WOLF: I should like to ask the presenters what therapeutic course they will follow in this case.

DR. VICTOR H. WITTEN: At our own institution, the New York University Post-Graduate Medical School, it is gratifying that the surgeons have learned to recognize the melanotic freckle and now accept the diagnosis. Furthermore, they have agreed to be conservative in their surgical approach and have avoided radical surgery. In this particular case, excision with a small but adequate border is planned so that the wound may be closed by primary suture and without graft.

Knowing Dr. Herman Beerman's interest in this subject, I sent for his review a Kodachrome transparency of the lesion together with a biopsy slide. He concurred wholeheartedly with the diagnosis and agreed with surgical excision, stating that he, personally, did not favor electrodesiccation of these lesions.

Diagnosis: Distinctive Exudative Discoid and Chronic Lichenoid Dermatitis in a Fifteen-Year-Old Boy. Presented by DR. JOHN GARB.

Diagnosis: Acrodermatitis Chronica Atrophicans Complicated by Bilateral Prickle-Cell Epithelioma: Surgical Removal and Successful Grafting of the Epithelioma. Presented by DR. JULIUS H. POLLOCK.

A Case for Diagnosis (Nodular Vasculitis? Panniculitis?). Presented by DR. JOHN GARB.

Diagnosis: Scleroderma in a Child? Presented by DR. ERNST. M. ROSENBAUM.

Diagnosis: Aneurysm of the Arch of the Aorta Simulating Superior Sulcus Tumor, with Angiocardiographic Studies. Presented by DR. CONARD STRITZLER.

CHICAGO DERMATOLOGICAL SOCIETY

Samuel M. Bluefarb, M.D., President
Frederick J. Szymanski, M.D., Secretary

March 19, 1958

Erythema Nodosum with Conjunctival Nodules. Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, and DR. JOSE LATONI (by invitation).

A 28-year-old Negro woman developed a "cold and sore throat" two weeks ago, which lasted several days. A week previous to admission, she noticed a tender "spot" on both legs and redness of the left eye. The lesions of both legs and eye are subsiding.

The patient was seen by the Eye Clinic on March 4, 1958. A diagnosis of bulbar conjunctival nodules secondary to erythema nodosum was made. Biopsy was performed on the eye lesion.

Presently, she is receiving tetracycline, 250 mg. q. i. d.; sulfisoxazole (Gantrisin) eye drops, and ophthalmic cortisone acetate.

Submitted for publication July 14, 1958.

Discussion

DR. JOHN GOLDEN (by invitation): Regarding the eye findings in these cases, what you get is a red eye and what you see on close inspection are nodules. In the eye there is a possibility of two diseases, one is iritis or iridocyclitis and the other is conjunctivitis.

This girl came in with painful red eyes. She had nodules in the area of the palpebral fissure. This ocular condition is very rare. There are only about two cases reported in the eye literature. A biopsy of these nodules was performed. As far as we could determine, there has never been a biopsy performed on these lesions previously.

The treatment consisted of fludrocortisone (Cortone) drops every two hours. The eye manifestations subsided when the skin lesions subsided. After the biopsy, the conjunctiva healed.

QUESTION: Is this a nodule, not a pterygium?

DR. GOLDEN: These are nodules, not pterygia. The nodules are on the inner canthus.

As far as the micropathology of the lesions themselves, it has never been described. The micropathology of this lesion was nonspecific. There was an angiomatous infiltrate with connective tissue proliferation.

Hidradenitis Suppurativa. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS (by invitation), and DR. JOSE LATONI (by invitation).

A 46-year-old Negro woman has had "irritation" on the axilla for the past two years. A week ago she noticed, for the first time, the appearance of suppurative "lumps."

The patient was placed on erythromycin, 500 mg., and prednisolone, 5 mg., q. i. d. for three days with remarkable improvement.

Discussion

DR. S. J. ZAKON: Dr. L. Goldberg, of Cincinnati, recently published a paper on the value of the combination of antibiotics and steroids. He used tetracycline combined with 8 mg. of steroid with some excellent results in hidradenitis suppurativa.

DR. THEODORE CORNBLEET: This combination of antibiotic and steroid has given us consistently good results. It should be emphasized that this method is only a holding action—it does not cure. Recurrence follows stopping of treatment.

DR. LEON GOLDMAN, Cincinnati: I should agree with Dr. Brunsting that the basic treatment is good surgery. We have seen improvement with steroid antibiotic combinations, but no persistent cure. Eventually for the severe case the problem is one of surgery. It requires an expert surgeon. It requires special knowledge of the disease and special interest and training in radical surgery of the axilla, perineal area, and scalp. In our series, we have had two complete scalp grafts. If any of you have tried to put a graft into an axilla and to get the graft to follow the undulating contours of the axilla and have the graft stay in, you will realize the difficulty of the procedure. In severe hidradenitis, after radical surgery, we have seen excellent results without recurrence during a prolonged period of observation of these patients through various hormonal difficulties. For incision of active abscess, if you incise in the direction of the lines of cleavage of axilla you will get a much better result.

DR. ALEXANDER BUCHHOLZ: We have controlled a case of hidradenitis suppurativa involving axillae, genitocrural fold, and nape of neck for the past 11 years by the administration of antibiotics. This man is a paraplegic and had the cutaneous disorder since 1939. Surgery was not done because of the paralysis.

DR. LOUIS BRUNSTING, Rochester, Minn.: There are a number of unanswered questions in connection with hidradenitis suppurativa, most of them concerned with the peculiar distribution of the lesions, chiefly in the apocrine sites, but the endocrine relationship is not proved. It is interesting to note that steroid hormones exert a suppressing effect on the disease. In men, the back of the neck is frequently involved; in women, never. In the earlier days, suppurative lesions in the axillae and groin were frequently confused with tuberculosis. Early, all solitary lesions may be treated by evacuation and the use of antibiotics and x-ray. In the more advanced cases, wide excision and plastic repair are the simplest solution in the long run.

DR. M. R. CARO: I should like to ask Dr. Brunsting if he has seen many cases of lymph stasis produced by obstruction in the axilla. In one of our cases of hidradenitis in the axilla operated upon recently there was a resulting lymph stasis of the arm.

DR. BRUNSTING: Since the advent of the sulfonamides and the antibiotics, we rarely see progressive lymphangitis and the progressive undermining ulceration which formerly led to deformity and lymphedema. Even with extensive surgery of the axilla or groin, lymphedema of the extremities as a consequence is a great exception.

DR. ZAKON: We have under our care now a man who had extensive surgery for hidradenitis suppurativa in the perineum. We found his γ-globulin reading to be low. We gave him 4 cc. of γ-globulin and his lesions improved. This is one instance where the patient apparently needed γ-globulin as a defensive mechanism.

DR. M. PAUL LAZAR: I came upon this problem suddenly several years ago. A patient who had hydradenitis had been exposed to poliomyelitis

and was given γ-globulin, after which his hidradenitis suppurativa went into a remission. He had had the problem for some 15 years, with many severe exacerbations and activity present most of the time. We continued treating him with γ-globulin, and he has stayed well for almost two years. He has had some difficulty, but it has never been severe. γ-Globulin will only give one protection found in the normal person. It is not an antibiotic, and sometimes people expect more protection than they should. With this in mind we have a number of people with hidradenitis suppurativa, as well as some other infectious conditions, and have given them γ-globulin at weekly intervals. Most of the people have normal γ-globulins. It is possible they do not synthesize antibodies well enough. A few of our subjects had low γ-globulin levels, and others were low normal. Some people are doing very well on γ-globulin, and after they stabilize we lengthen the period between injections. The study has not been finished, so final evaluations cannot be made. There is perhaps hope for a certain number of patients; γ-globulin has been used in association with one of the antibiotics, but we have used just γ-globulin. Some patients have done well, and in others it has had no effect.

DR. WALTER C. LOBITZ JR., Hanover, N. H. (by invitation): In the past year or two we have been interested in an increasing incidence of pyoderma in the axilla that is more acute than the classical chronic hidradenitis. We are having the same problem as most centers with Staphylococcus pyogenes var. aureus skin infections. It does not seem to matter for what the patient is admitted to the hospital or on what service. If these patients do develop some type of pyoderma the commonest location is in the axilla or groin. They start off looking very much like a classical hidradenitis without much discharge and with a firm tender nodule. Some will involute spontaneously, and some need the antibiotic of choice systemically before they will subside. I do not know the significance of the location of this pyoderma. But one wonders whether classical hidradenitis may start this way. I should also be interested if such a location on the skin of "hospital pyoderma" is peculiar to New England or is just a generally observed problem?

Polymorphous Light Eruption. Presented by DR. ALBERT H. SLEPYAN.

A white woman, aged 50, states that since early childhood she can recall an eruption appearing on her arms and hands during the summer months. In early adult life, beginning in the teens up to age 30, she recalls being able to expose herself to the sun without breaking out. Since that time she has been unable to sit in the sun without hives appearing.

She was first observed in January, 1949, and has been seen periodically with an eruption appearing on her face, arms, and in areas exposed to sunlight. At times the eruption over the face appeared as isolated pinhead- to match-head-sized papules. At other times the lesions appeared grouped or in clusters of papules. Occasionally, a fingernail-sized plaque of erythema was noted, and at times, the lesions suggested superficial vesiculo papules.

Examination today: Over the right cheek extending upward to the temple area there are grouped erythematous papules, dull reddish brown in color. Some of these papules are match-sized and are indurated. There are only a few isolated papules seen on the left side of the face. Over the dorsum of the hands there is an occasional firm hard papule with areas of excoriation. Freckling and depigmentation with atrophy is seen over both forearms and extending up to the arm.

Laboratory findings, March 28, 1957: hemoglobin 14.4 gm. (94%); white blood cells 6,900, with 70% neutrophils, 2% eosinophils, 27% lymphocytes; red blood cells 4,940,000.

Calcium-pantothenic acid levels, bound-free ratio: Feb. 15, 1955, 1:5; May 24, 1956, 5:8.

No uroporphyrin was found; section from biopsy specimens taken on Feb. 15, 1955, and Feb. 24, 1958, shown under the microscope.

Discussion

DR. LOUIS BRUNSTING: It seems very evident this patient has a photosensitive eruption of the exposed surfaces, but I doubt that she is porphyric. It is conceivable that the cystic lesions over the malar prominences may be a late consequence of the photosensitive effect. In considering the differential diagnosis, it is well not to mention in the hearing of the patient the possibility of lupus erythematosus because of the psychologic reaction which develops.

DR. LEON GOLDMAN, Cincinnati: The late Nelson Paul Anderson used to say "BAIK, Boy, am I konfused."

In our study of lymphadenosis cutis benigna, especially of the disseminate type, such a history of light sensitivity has not been obtained. There has been no evidence of visceral malignant lymphoma developing in these patients as yet. Bafverstedt still has to review his original series. There have been malignancies developing secondarily in the skin, such as dermatofibrosarcoma protuberans or squamous; also, there have been malignancies of the stomach and pelvis in these patients. Bafverstedt told us of one case reported from Germany where a patient had malignant lymphoma. This is the first case I have observed in whom a light-

sensitivity produced lesions which "developed into" these lesions now present.

DR. PAUL WEICHELBAUM: About four years ago I presented a case of light sensitivity with infiltrated patches on the exposed skin. The diagnosis of the pathologist was possible lymphoma. We could find no evidence of systemic involvement. He cleared on chloroquine (Aralen). Since then I have seen other cases with similar involvement after exposure to sun. Another one of these cases was controlled by chloroquine.

DR. A. J. REICHES, St. Louis: Dr. Rothman's suggestion that there are in all probability two conditions present is very logical. I believe that those cases of light sensitivity which are similar clinically and histologically to discoid lupus erythematosus are in all probability a part of the lupus erythematosus syndrome.

DR. M. PAUL LAZAR: One of the patients that was reported by Dr. Jessner is someone I know. This is probably 10 years after he was biopsied, and the eruption has cleared without any therapy. He has had several recurrences, but they have cleared without further therapy. At one time he was given chloroquine without any change in the lesion.

DR. THEODORE CORNBLEET: I should like to see elastic tissue stains of sections. I saw vesicles on prominences of the hands subject to trauma, and these changes added to the atrophic ones suggest the dystrophic form of epidermolysis bullosa. Another thought on this patient is light-induced urticaria. I have a patient with such a condition, in whom the wheals occur at only certain sites—a kind of fixed eruption.

DR. S. M. BLUEFARB: It is my impression that this patient has lymphadenosis benigna cutis. I belive that sunlight might be a traumatic factor. The histologic picture is characteristic of lymphadenosis benigna cutis.

DR. A. H. SLEPYAN: Some of us have been confused with this pattern for just one afternoon. I have been puzzled with her for over 10 years. The patient's eruption has shown a tendency toward polymorphism of the lesions. At times, they suggest areas of lupus erythematosis, and at other times there are discrete papules which suggest a tendency toward vesiculation. On occasion, it appears as though the lesions were those of lymphocytic infiltration of the skin. It is most peculiar that, in 1955, a biopsy showed a sarcoidal structure, and now the more recent biopsy shows the structure that we associate with Spiegler-Fendt sarcoid. It is rather strange that in this instance the reticulum cells appear as the outer structure of the "germinal body" with the lymphocytes making up the center. I do not know what this alteration indicates, if anything. As far as therapy over the years, there have been periods when she would respond to quinine and the antimalarial drugs. At the present time, she has not responded to chloroquine.

Lipoid Proteinosis. Presented by DR. BRIAN POTTER (by invitation) and DR. PAUL WEINMANN (by invitation).

A 38-year-old white housewife (reported by Tompkins and Weinstein *Ann. Int. Med.* 41:163, 1954), previously presented to the Chicago Dermatological Society in 1950 with the same diagnosis, was first seen at the University of Chicago Clinics in 1943. Onset of her disease began shortly after birth, with infiltrative lesions developing on the mucous membranes of the mouth and the development of hoarseness at the age of about 9 months. Similar lesions also developed on the tongue and pharynx. Skin biopsy in 1943 confirmed the clinical diagnosis of lipoid proteinosis. The patient was given Lipocaic, a lipotropic pancreatic preparation, for a period of three years (1943-1946), as well as liver extract and syrup of choline. During this time she developed discrete small papules along the free border of the upper eyelids and both axillae and multiple small yellowish macules on the upper trunk. The patient again took Lipocaic, from 1950-1951, during which period the hoarseness decreased somewhat. Within the last year the patient has been undergoing speech therapy and taking a proprietary "nutritive supplement" on her own. On March 5 a trial of Arcofac (cholesterol-lowering factor, Armour), 1 tablespoonful (15 ml.) t. i. d., was begun.

Family history and physical examination are otherwise not remarkable.

Biopsy of a papule from the left axilla shows the following: Eosinophilic homogenous material is present in masses in the upper corium, raising the epidermis in domes and causing secondary atrophy of it. Relative acanthosis separates each mass from the next. The areas are edematous, fissured in places, and associated with a moderate proliferation of fibroblasts. Similar hyaline material surrounds the eccrine glands, but the apocrines are relatively unaffected. The intervening corium appears normal. This material is strongly PAS-positive but negative for amyloid. Fat stain on frozen sections is positive.

Lipid analysis of blood serum revealed values within normal ranges for total lipids, total fatty acids, lipid phosphorus, total cholesterol, and ratio of free to esterified cholesterol.

Other laboratory studies, including chest x-ray, electrocardiogram, hemogram, urinalysis, STS, plasma proteins, glucose tolerance curve, liver biopsy, and liver-function tests, were all within normal limits. Electrophoresis of plasma proteins was not remarkable.

Lipoid Proteinosis. Presented by DR. BRIAN POTTER (by invitation) and DR. PAUL WEINMANN (by invitation).

A 37-year-old white woman was first seen at The University of Chicago Clinics in 1945, complaining of hoarseness and skin lesions of the face and neck, present since early childhood. She was presented in this Society in May, 1945. The skin lesions consisted of yellowish plaques over the elbows and knees, as well as thickening of the mucous membranes of the lips, buccae, pharynx, and vocal cords. She was given syrup of choline and placed on a low phospholipid diet without amelioration of symptoms. In 1950, she started taking Lipocaic for one and one-half years with apparent moderated initial improvement, evidenced by reduction of the lip and tongue infiltrations. In December, 1957, a large plaque was surgically removed from the right knee, since this had interfered with locomotion. Histological sections and lipid analysis from this plaque are presented. Family history and general physical examination is otherwise noncontributory.

There is eosinophilic hyalinization of the upper corium associated with a proliferation of fibroblasts. Deep to this the collagen bundles have lost their normal fibrillae appearance. Blood vessels and particularly sweat glands are surrounded by marked hyaline rings. Frozen sections show fat to be present, stained by Sudan IV. In paraffin sections the material is strongly PAS positive.

Lipid analysis of the excised plaque of skin revealed an unusually high amount of unsaponifiable material (38.6% of the total lipids). Only a small fraction of this, 8%, could be accounted for by sterols. This unsaponifiable fraction is now being analyzed. Also, in contrast to earlier data, the phospholipid content was found to be low (10.6% calculated as lecithin), rather on the low side of normal values.

A glucose-tolerance test in 1945 showed a diabetic curve, but a repeat examination in 1953 was within normal limits.

Other laboratory studies, including chest x-ray, upper gastrointestinal series, electrocardiogram, basal metabolism rate, urinalyses, hemogram, STS, plasma proteins, sternal puncture, liver biopsy, and liver-function tests, were all within normal limits. Electrophoretic pattern of serum proteins is not remarkable.

The Figure is a picture taken in 1945.

Summary of Data

Lipid Analysis, Skin	Gm/100 Gm. Dry Weight	% of Total Lipid	Values Reported in Literature
Total lipid	5.6	—	
Total fatty acids	3.03	54.2	86.0 *
Total nonsalponifiable	2.16	38.6	
Lipid phosphorus	0.024	0.43	76.0 *
(as lecithin)	0.59	10.6	22.0 †
			Normal: 10-30
Total sterols	0.45	8.0	16.0 *
Free fast acting	0.01	0.2	
Free cholesterol	0.33	5.9	
Ester cholesterol	0.11	1.0	

Lipid Analysis, Serum	(1945)	(1958) Mg/100 Ml.	Normal Range
Total lipid	724, 729	800	360-820
Total fatty acids		320	190-600
Lipid phosphorus		9.0	6.1-14.5
Total cholesterol	250, 227	204	100-320
Ratio free/total		0.38	0.24-0.32

* Montgomery, H., and Havens, F. Z.: *Arch. Otolaryng.* 29: 650, 1939.

† Hansen, P.: *Arch. f. Dermat. u. Syph.* 175: 618, 1937.

Discussion

DR. BRIAN POTTER (by invitation): We have done some more work on these cases since they were reported before. The frozen sections were stained with Sudan IV and show fat to be present. On extraction of this fat with solvents, it was found that while the total lipid (as % of dry weight of tissue) was within the normal range, the amount of phospholipid was low (10.6% of total lipid), while there was an appreciable amount of nonsaponifiable matter (38.6% of total lipid).

However, the other sections were made from paraffin-embedded tissue, fat being dissolved out in the process, and yet pathologic material is still present and is strongly PAS positive. This undoubtedly represents polysaccharide, though it may be combined with protein, in which case it would be called glycoprotein. On the basis of these findings, I think the name of the disease should be lipid polysaccharidosis.

Secondary Syphilis. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS (by invitation), and DR. JOSE LATONI (by invitation).

Congenital Dystrophy of Nails. Presented by DR. DAVID V. OMENS, DR. STANLEY HUFF, DR. HAROLD D. OMENS (by invitation), and DR. HASSAN M. YAZDI (by invitation).

Scleredema? Panniculitis? Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and DR. HASSAN YAZDI (by invitation).

Fibromyxosarcoma (Basal-Cell Epithelioma?) Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, DR. STANLEY HUFF, and DR. MARTIN L. GECHT (by invitation).

Morphea-like Epithelioma: Cleatrizing Basal-Cell Epithelioma? Presented by DR. ARTHUR F. STILLIANS.

Radium Therapy to a Squamous-Cell Carcinoma in an Area of Chronic Discoid Lupus Erythematosus. Presented by DR. I. MYRON FELSHER.

Healed Tertiary Syphilis. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS (by invitation), and DR. MARTIN L. GECHT (by invitation).

Tertiary Syphilis. Presented by DR. DAVID V. OMENS, DR. HAROLD D. OMENS (by invitation), and DR. HASSAN YAZDI (by invitation).

Hemangioendothelioma. Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and DR. MARTIN L. GECHT (by invitation).

Sarcoidosis. Presented by DR. SAMUEL M. BLUEFARB, DR. SILAS WALLK, and DR. MARTIN L. GECHT (by invitation).

Sarcoid. Presented by DR. ALFRED B. FALK, DR. FREDERICK J. SZYMANSKI, and DR. ROLAND S. MEDANSKY (by invitation).

Verrucous Hypertrophy of the Legs: Localized Amyloidosis? Localized Myxedema? Presented by DR. THEODORE CORNBLEET, DR. SIDNEY BARSKY, and DR. HASSAN YAZDI (by invitation).

Erythema Perstans Faceii? Presented by DR. JOHN B. HAEBERLIN JR. and DR. J. D. MAJARAKIS (by invitation).

Case for Diagnosis (Tuberculosis Collequativa?). Presented by DR. IRENE NEUHAUSER.

Multiple Compound Nevi in Distribution of Fifth Nerve. Presented by DR. BRIAN POTTER (by invitation) and DR. PAUL WEINMANN (by invitation).

Case for Diagnosis (Solid Edema and Erythema Nodosum?). Presented by DR. MARCUS R. CARO (by invitation), DR. GEORGE FLEMING (by invitation), and DR. ROLAND S. MEDANSKY (by invitation).

Bacterid? Presented by DR. SAMUEL J. ZAKON and DR. JOHN B. HAEBERLIN JR.

CHICAGO DERMATOLOGICAL SOCIETY

April 16, 1958

Solid Edema. Presented by the STAFF of the UNIVERSITY of ILLINOIS RESEARCH and EDUCATIONAL HOSPITAL.

The patient was presented at the March meeting as a case of solid edema of the face with associated erythema nodosum on the extremities. At that time, in the discussion, it was suggested that the background here might be that of a malignant lesion of the antrum or a possible lymphoma.

Since the last presentation, laboratory examinations, consisting of roentgenograms of chest and nasal sinuses, complete blood cell count, urinalysis, antistreptolysin titer, and serum proteins, were within normal limits. Patient developed a severe myositis involving the gastrocnemius muscles of both legs since his admission to the hospital.

Nearly two weeks ago treatment was instituted consisting of erythromycin, 3.0 gm. daily, and the lesions on the face have undergone considerable involution with almost complete softening of the upper lip. The myositis has improved and the lesions of erythema nodosum have disappeared completely. His temperature has remained normal since therapy was instituted.

The patient is being presented again to show progress in his condition.

Submitted for publication July 17, 1958.

Discussion

DR. CLARK W. FINNERUD: As I remember this patient from a month ago (I think he was presented in March), he has rather dramatically improved, at least in the lower part of his face. A few cheek areas are still very hard. He himself feels that as a result of the antibiotics he has been receiving he has made very definite progress. During my long stay at Rochester I saw a number of these patients who had been treated with boiling-water injections where everything else had failed. Two

of them greatly impressed me. The Plastic Surgery Department apparently sometimes gets excellent results from such injections.

DR. MILTON ROBIN: You may recall several months ago I presented a patient of my own who had solid edema of both lower lids. It was suggested that hyaluronidase be injected into the affected areas. I have tried this therapy with no success. The only drugs that give temporary relief are the steroids.

Melanotic Freckle of Hutchinson. Presented by DR. STEPHEN ROTHMAN and (by invitation) DR. BRIAN POTTER.

In 1954, the patient first noticed that a dark brown spot on the left malar eminence was increasing in size. A biopsy was made and reported as benign lentigo in July, 1954, when the lesion measured 10×17 mm. It continued to enlarge for the next three years and in July, 1957, measured 15×30 mm. The macule at that time extended to within 5 mm. of the outer canthus and contained in the center a sharply circumscribed rectangular 4×5 mm. darker brown macule.

The lesion was almost entirely removed in a three-stage plastic operation, and the biopsies made at each stage are presented. No further surgery has been performed since September, 1957, and there has been no objective change in the lesion since his postoperative visit in November.

On examination there extends down from the outer canthus of the left eye a linear surgical scar 38 mm. in length. At the lower end of this is a 2 mm. diameter brown macule and 12 mm. above the latter a pinhead-size brown macule is present in the scar. There are three circumscribed pigmented macules around the upper pole of the scar and a lighter brown, more diffuse area between these and the outer edge of the lower eyelid.

Sections from the first stage excision show a junctional increase in a number of pigmented clear cells along the epidermis and superficial parts of the hair follicles. This proliferation is most marked in one area related to a hair follicle, but the cell nuclei are small and the change is confined to the epidermis. Circumscribed groups of epithelioid cells within the corium below this area are seen on recuts to be cross sections of hair matrix.

Sections from the second and third stages show only slight junctional increase in number of melanocytes.

The patient is presented with the request for therapeutic suggestions. The plastic surgeon feels that further excisions would require rather major plastic repair.

Discussion

DR. S. W. BECKER JR.: The melanotic freckle of Hutchinson is a clinical but not a pathologic entity. Hutchinson used the term to designate slow growing macular pigmented lesions on the face; histologically these lesions were found to be benign lentigo, pigmented basal-cell carinoma, or melanoma.

Both biopsy specimens from this patient show benign lentigo. There is proliferation of melanocytes with clusters of these cells at the dermoepidermal junction. These cells are actively forming melanin. I could not find any nevus cells in these preparations.

The problem in this patient is one of prognostic guessing. A proliferating melanocyte will either become a benign nevus cell or a malignant melanoma cell. This lesion has formed no nevus cells, has recurred after surgical removal, and has continued to grow. I feel that it will eventually become a frank melanoma. This lesion should be completely removed surgically.

DR. H. M. BULEY, Champaign, Ill.: I should like to support what Dr. Becker just said. During the past 20 years I have had the opportunity to observe the course of a melanotic freckle on the cheek of an elderly lady. In 1939, the lesion was about silver-dollar in size. It was biopsied, and the diagnosis of lentigo maligna was made by the late Dr. Fred Weidman. Surgical removal was then advised but refused by the patient. Since then the lesion spread slowly over the left side of the face and extended downward over the mandible to the neck. Only five or six years ago a few lenticular to cherry-sized nodules developed in the central portion of the cheek, some of which were excised by a surgeon. The histological finding was that of a typical melanoma. I believe, therefore, that in spite of its extremely slow growth at times, a melanotic freckle is a malignant lesion from the onset and should be treated as a melanoma; that is, removed radically as early as possible.

DR. JULIUS GINSBERG: I should like to ask Dr. Becker whether he thinks radical removal is indicated.

DR. BECKER: I do not think enucleation of the eye is necessary. A plastic surgeon should remove the lesion and try for the best cosmetic result that can be obtained.

DR. DAVID W. KERSTING, Milwaukee: Dr. Becker's explanation of the dynamics of this is interesting. However, in one section there is a focus of cells which is described in the protocol as a cluster of epithelioid cells involving the hair follicle. I did not think these cells were histiocytes. I thought they were large melanocytes and that, therefore, the lesion should be removed completely.

DR. BRIAN POTTER (by invitation): As Dr. Kersting noted, in the original sections of the first excision there are groups of what I should have said were epithelial, not epithelioid, cells in the

corium. However, further sectioning of the block shows that these cells belong to a hair follicle. If Dr. Kersting will accept this, then all who have studied the sections are agreed that the changes are junctional and confined to the epidermis and hair follicles. I interpret the process as histologically benign but extraordinary clinically and agree with Dr. Becker that one has to guess at the outcome.

Urticaria Pigmentosa (Mastocytosis) of Thirty-Nine Years' Duration. Presented by DR. S. M. BLUEFARB, DR. J. HASEGAWA (by invitation), and DR. F. DUNLAP (by invitation), from Northwestern University Medical School and the V. A. Research Hospital.

In 1919, soon after discharged from the armed service, the patient first noted a pigmented "rash" all over his body. This had not bothered him, and he has not had any extensive treatment for it. From Dec. 14, 1950, to Jan. 8, 1951, the patient was hospitalized at Dwight V. A. Hospital for chronic bronchitis, emphysema, and incidentally for a generalized rash. Biopsy specimens from the back and right forearm showed a diffuse infiltration with lymphocytes, rare plasma cells, and some histiocytes irregularly arranged and extending almost into the subcutaneous tissue. The diagnosis was chronic dermatitis, abnormal pigmentation. X-rays of the chest and right shoulder were normal.

He was readmitted to Dwight V. A. Hospital from July 22, 1955, to Sept. 16, 1955, for recurrent dyspnea and chronic cough. No biopsies were done. X-ray of the chest was normal. The dyspnea persisted and suddenly became worse on March 3, 1958. He traveled by train from southern Illinois to Chicago and was admitted to the medical service of the V. A. Hospital on March 5, 1958, with a provisional diagnosis of obstructive emphysema and pneumonia.

Physical examination showed an emphysematous type chest, intercostal retraction on inspiration, respiratory rate of 30 per minute, hyperresonance to percussion, rhonchi throughout the chest. There were questionable hepatomegaly and splenomegaly. A portable x-ray of the chest showed moderately marked accentuation of the hilar markings with, however, no definite areas of active pneumonitis.

The patient was first seen by the Dermatology Section on March 10, 1958, while still being treated in a respirator. Biopsies performed March 12, 1958, showed marked mast-cell infiltration in the corium, especially in the perivascular areas. Subsequent studies showed the following findings:

1. Normal iliac crest marrow examination except for clumps consisting almost entirely of mast cells.

2. Peripheral blood: White blood cells 6,500; red blood cells 3,530,000; hemoglobin 10 gm.; 34% hematocrit; normal platelet count; 11% band cells; 79% segmented cells; 7% lymphocytes; 2% monocytes; 1% eosinophils; anisocytosis, poikilocytosis; slight hypochromia; reticulocytes 2.6%; bleeding, coagulation, and clot retraction normal.

3. Fasting blood sugar 90 mg. %; 2 hours after glucose 162.5 mg. %.

4. Anteroposterior views of the right and left humerus and also the right and left femurs reveal a mottled ground-glass appearance in the proximal thirds of the humeri and also in the intertrochanteric regions and distal ends of the femurs. Anteroposterior and lateral views of the lumbosacral spine and also an anteroposterior view of the pelvis, including both hip joints, reveals a mottled ground-glass appearance of the spine and also the pelvic bones.

5. Electrocardiogram showed only nonspecific ST and T changes.

Discussion

DR. S. M. BLUEFARB: One does not find serotonin in mast cells of human beings, but it does occur in mast cells of the rat.

DR. ALLEN L. LORINCZ: Although it has been reported that skin rich in mast cells as occurs in urticaria pigmentosa lesions of the nontelangiectatic type does not contain serotonin (Sjoerdsma, A.; Waalkes, T. P., and Weissbach, H.: *Science* 125: 1202, 1957), I am not aware of such analyses for serotonin in lesions of the adult or telangiectatic type of urticaria pigmentosa. Possibly the mast cells in these telangiectatic lesions may be of different type and contain serotonin, as do the mast cells of rat and mouse skin.

DR. S. M. BLUEFARB: The report from the Sjoerdma's group at the Public Health Service indicated that they were unable to demonstrate serotonin in human mast cells.

DR. THEODORE CORNBLEET: It seems that we have to learn how to break the mast-cellular bond holding some of its physiologically active constituents. About three years ago I published the results of our experiments in which we tried to separate the heparin from lesions of urticaria pigmentosa. Either the heparin was physiologically inactive, or we could not release it. The same problem may be present with regard to serotonin.

DR. J. HASEGAWA (by invitation): We had not considered serotonin as a factor. So far as I am aware, the demonstration of serotonin has only been done in rats and mice. The work was done by Benditt and others. We shall certainly make an effort to examine the urine for serotonin. As you all know, it is almost impossible to measure plasma serotonin because the material is present in the platelets. It is almost impossible to draw the blood and centrifuge it without breaking the platelets. We have attempted to isolate mast cells in this

patient's sputum and have failed so far. Bronchoscopy is not indicated because the patient becomes cyanotic very rapidly due to emphysema.

Subcorneal Pustular Dermatosis. Presented by Dr. Theodore Cornbleet, Dr. Sidney Barsky, and Dr. J. Latoni (by invitation).

A 34-year-old Negro woman has been developing skin lesions for the past five years with remissions and exacerbations; never completely clearing. Her first lesions appeared on the thighs followed by similar ones on the axillae and neck. Some of the lesions have been moderately pruritic. No history of drugs was given, and no involvement of the mucosa was noted.

The patient was admitted to Cook County Hospital on March 28, 1958, with a superficial pustulovesicular dermatosis of serpiginous borders with some coalescence and patch formation. Sulfapyridine was given for a week (0.5 gm. q. i. d.) with prompt and almost complete clearing of the lesions.

Laboratory Findings: Blood chemistry, complete blood cell count, urine, and serology were normal. Biopsy specimen is presented.

Discussion

Dr. Peter Samman, London, England (by invitation): This was an interesting case. The only cases I have seen had the characteristic picture of erythema with pustules around the edge which tends to increase outward. The histology is always below the horny area. These cases respond to larger doses of sulfonamide than used in the case presented.

Dr. Adolph Rostenberg Jr.: I should like to ask Dr. Samman if he has found any relation to impetigo herpetiformis. It seems to me some of the cases are very much like that disorder.

Dr. Samman: The question is often raised of the relationship to impetigo herpetiformis. One peculiar fact is that impetigo herpetiformis is usually fatal in the pregnant woman, but in women of 50 to 60 years of age it is much milder.

Dr. Frederick J. Szymanski: In this case and in a few others we have studied, we have seen acantholytic cells. Is this feature emphasized by the group in England?

Dr. Samman: I cannot discuss the acantholytic cells. When the first case was shown before the French Society in England it was thought to be moniliasis, but the French dermatologists who presented the original cases were sure it was not moniliasis.

Familial Benign Chronic Pemphigus. Presented by Dr. R. E. Bloom, Muskegon, Mich.

Vesicular Lichen Planus with Nail Changes. Presented by Dr. Paul K. Weichselbaum.

Idiopathic Multiple Hemorrhagic Sarcoma (Kaposi). Presented by Dr. Otto C. Stegmaier, Davenport, Iowa.

Mycosis Fungoides. Presented by Dr. John B. Haeberlin Jr. and Dr. Stefan Bielinski.

Nummular Eczema? (Psoriasis?) with Arthritis. Presented by Dr. Herbert Rattner and (by invitation) Dr. Arthur Norins.

Secondary Carcinomatous Deposits by Lymphatic Extension. Presented by Dr. Stephen Rothman and Dr. Brian Potter (by invitation).

Lymphosarcoma Cutis. Presented by Dr. S. M. Bluefarb; Dr. Silas Walke, and Dr. J. Latoni (by invitation).

Incontinentia Pigmenti (Bloch-Sulzberger Syndrome). Presented by Dr. David V. Omens, Dr. Harold D. Omens (by invitation), and Dr. Martin L. Gecht (by invitation).

Bullous Erythema Multiforme. Presented by Dr. Theodore Cornbleet, Dr. Sidney Barsky, and Dr. Hassan Yazdi (by invitation).

Metastatic Carcinoma. Presented by Dr. David V. Omens, Dr. Harold D. Omens (by invitation), and Dr. Hassan Yazdi (by invitation).

Pustular Psoriasis Treated with Kenacort. Presented by Dr. S. M. Bluefarb, Dr. Silas Walke, and Dr. Hassan Yazdi (by invitation).

Allergic Vasculitis Associated with Acute Monocytic Leukemia. Presented by Dr. Samuel M. Bluefarb, Dr. Silas Walke, and Dr. Martin L. Gecht (by invitation).

Nail Dystrophy. Presented by Dr. Theodore Cornbleet, Dr. Sidney Barsky, and Dr. J. Latoni (by invitation).

DETROIT DERMATOLOGICAL SOCIETY

Dr. George B. Sexton, London, Ont., Canada, President
Dr. Alice E. Palmer, Secretary
Dr. Robert E. Burns, Recorder

Oct. 8, 1958

Allergic Cutaneous Vasculitis. Presented by Detroit Receiving Hospital.

A Negro woman 58 years of age began to develop nonpruritic red spots on her legs five months ago. There was no history of preceding infections or fevers; there was, however, a complaint of vague leg pains of indefinite duration. Drug intake consisted of occasional epsom salts, cream of tartar, and herb "tea." General physical examination is not contributory. Cutaneous examination reveals pinhead- to pea-sized slightly elevated, brightly

Submitted for publication Dec. 5, 1958.

erythematous papules on the legs and lower thighs. These are not obliterated by diascopic pressure. On the dorsum of the feet are excoriated, lichenoid papules and sparse, scattered vesicles, and bullae may be found on the lower legs.

Laboratory findings were as follows: WBC 7,400, Hgb. 13.3 gm., ESR 45 mm. in one hour; urinalysis, sugar negative; albumin trace; microscopic, a few RBC's and WBC's and epithelial cells and bacteria seen.

Histology: "The epidermis and papillary zone show no significant change. Several arterioles in the midcorium show eosinophilic trabeculation of their walls and are surrounded by polymorphonuclear infiltrate with many pycnotic and fragmented nuclei. Small venules or perhaps lymph vessels are surrounded by similar infiltrate. Other vessels show swollen endothelia and increase of perivascular fixed tissue cells. There is edema between the collagen bundles, and Orcein-Giemsa stain shows amorphous basophilic material in these areas. Similar changes are present around perifollicular capillaries. These are scattered eosinophiles. Microscopic diagnosis: allergic vasculitis."

Sensitivity Angiitis. Presented by Dr. Herschel Zackheim.

A white woman, 31 years of age, developed painful swelling of her left hand and wrist in February, 1958. This was treated as a tenosynovitis, with splints, bandaging, and a black salve. A week later large blisters appeared on this wrist, followed by vesicles and hemorrhagic bullae on both hands and wrists as well as tender hard subcutaneous papules on the forehead. A tentative diagnosis of contact dermatitis due to the salve was made; however, persistence of the bullae together with the development of general weakness led to her admission to hospital on March 16, 1958.

In hospital she developed vesicles and bullae on the hands and feet and papules on the face. Pruritic wheals appeared and erythematous macular patches on the trunk and extremities. In addition, she complained of painful swellings of the hands and feet, migrating muscle and joint pains, headaches and general weakness.

She was first treated with triamcinolone (Aristocort), 12 mg. daily, and diphenhydramine (Benadryl), 50 mg. q. i. d., without effect. Ten days later treatment was changed to methylprednisolone (Medrol), 12 mg. daily, with marked improvement of the skin lesions and the musculoskeletal symptoms. Following discharge from hospital on April 16, 1958, it was necessary to maintain her on between 16 and 20 mg. of methylprednisolone, for if the dosage were lowered urticaria and blisters appeared. Since September she developed peculiar linear raised lesions in the antecubital spaces.

Past history: The patient had hay fever for many years and many recurrent bouts of urticaria, necessitating hospital care at age 19. She was delivered of a normal full-term girl Dec. 9, 1957. She took 20 Emperin and codeine tablets between the time of delivery and the appearance of the eruption in February.

Laboratory findings: Blood cell count has shown a leukocytosis from 14,000 to 27,000, with a persistent eosinophilia, even with steroids, from 22% to 54%. L. E. studies were negative. Urinalysis was negative except for a temporary leukocytosis. Blood chemistries: bilirubin, cholesterol, proteins, sugar, and urea N within normal limits; serum amylase 44 units (normal 80-180); stools negative for ova and parasites; bone marrow showed marked predominance of eosinophils but no leukemia; ECG normal; chest x-ray showed mild peribronchial thickening of uncertain etiology.

Histology: Subcutaneous nodule forehead: "Eosinophilic infiltrate around all medium-sized blood vessels, infiltrate is not heavy but is almost 100% eosinophils. Diagnosis: Deep-seated eosinophilic vasculitis (?) drug reaction (Dr. Pinkus)."

Fresh vesicle of hand: "Moderate number eosinophils in vesicle; marked infiltration by eosinophils about small vessels in lower corium; moderate thickening of walls of small arterioles but no necrosis of the walls."

Raised red papule side of face: "In midcorium there is marked eosinophilic infiltration which separates collagen bundles and surrounds nerves and vessels; occasional small vessels are completely occluded. Diagnosis: Sensitivity angiitis of the skin (Dr. Linn, Beaumont Hospital)."

Linear lesion antecubital space: "Multiple foci of necrosis in the middle and deeper corium, consisting of eosinophilic and broken up collagen containing many pyknotic nuclei, suggesting that there was first an invasion by leukocytes. These foci are surrounded by a mild granulomatous reaction consisting of histiocytes in epithelioid arrangement, a few giant cells, and some eosinophils. I did not see remnants of any sizable vessel in the necrosis. I believe these changes represent a severer stage of the sensitivity reaction, but I cannot call it periarteritis nodosa because I can not prove that the necrosis involves blood vessels (Dr. Pinkus)."

Discussion

Dr. Patrick Wilson: The first patient showed a bilateral polymorphic eruption of the lower extremities, comprising macules, nodules, slightly infiltrated bullae, necrotic lesions, and varioliform scars. There was no antecedent polyarthritis, which is said to be usual. There was no evidence of focal infection, also said to be rather characteristic. The histopathology I thought characteristic of the syndrome and included the findings that are supposed to be diagnostic—or almost so—diffuse fibrinous degeneration of the walls of the small blood ves-

sels and perivascular tissues, diffuse polymorphic infiltrate with large numbers of pyknotic nuclei and occasional disseminated eosinophils. I felt that this case showed most of the features of the syndrome designated allergic cutaneous vasculitis.

The second case was more typical in some respects, although there were some atypical features. This patient experienced polyarthritic onset; there was an atopic background common in cases of this type; again a polymorphic eruption with essentially the same types of lesions as that noted above except that some had more tendency to urticaria. One unusual aspect of this case is the almost complete absence of lesions over the legs. While the patient showed minor involvement on the feet and ankles, there was little or no involvement on the legs. The lesions involving the antecubital areas were extremely unusual, and in searching through the literature, which I had the opportunity to do this past week, I could find no description of lesions resembling these. They may perhaps have been modified somewhat by steroid therapy. Angiokeratoma-like lesions have been described, and I wonder if these may have resembled lesions of this type prior to institution of treatment. Apparently necrotic and hemorrhagic lesions have been present, although they are not today. The pronounced leukocytosis I think is unusual. In most cases, the white blood cell count is normal or slightly elevated. I think the pronounced eosinophilia in the peripheral blood is also unusual. Histologically again I felt the specimens were quite typical of the condition designated allergic cutaneous vasculitis.

Dr. Coleman Mopper: When I saw the first case, which was diagnosed as allergic cutaneous vasculitis, I could not rule out an allergic response to cold agglutinins. Unfortunately there was no study performed to determine cold agglutinins. I feel that this should be done. She should be investigated for cryoglobulins as well.

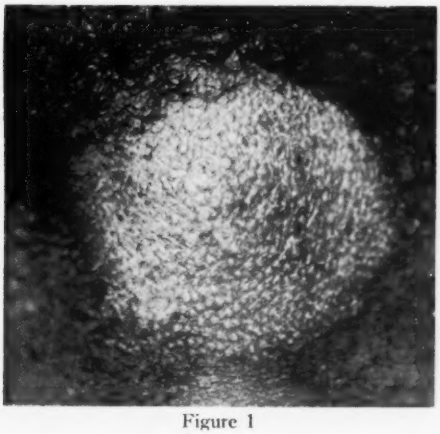


Figure 1

Dr. Herschel Zackheim: Clinically the hard subcutaneous papules on the forehead and the linear raised streaks in the antecubital spaces are very unusual. The antecubital lesions developed while she was on steroids. The patient failed to respond ot triamcinolone but showed good response to methylprednisolone. She needs to be on about 16 mg. of methylprednisolone daily; otherwise there is a prompt recurrence of erythematous blotches, wheals, and blisters. Luckily there has been no evidence to date of involvement of any internal organ, such as occurs in a true necrotizing angiitis. Pathologically, the unusual features was the tremendous eosinophilic infiltrate, from the papule on the face, not only around the blood vessels but throughout the cutis, and the peculiar deep necrosis apparently of collagen and inflammatory cells from the biopsy specimen of the antecubital lesion. No fibrinoid necrosis of blood vessels has been found.

Alopecia Mucinosa. Presented by Detroit Receiving Hospital.

A Negro youth of 16 years developed a painless, slightly pruritic, silver-dollar-sized swelling on the nape of the neck a year ago. Gradually hair was lost from this area, and six months later alopecia developed on the left eyebrow, on the left occipital scalp, and on the pubic area. Later small plaques of follicular papules were found on the posterior aspect of each arm and upon the extensor surface of the left knee.

A well-demarcated boggy swelling is found on the nape of the neck (Fig. 1). This is hyper-

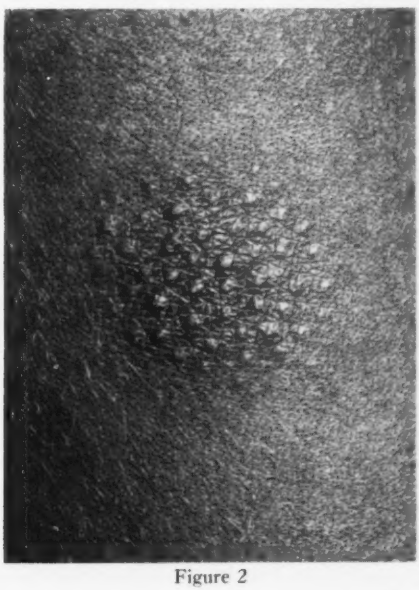


Figure 2

pigmented, slightly lichenified, and hairless. The left side of the occiput shows some alopecia. The left eyebrow and the pubic areas display well-demarcated patches of alopecia and follicular papules. On the posterior aspect of the arms (Fig. 2) and on the extensor aspect of the left knee are found well-defined plaques of follicular papules. Woods-lamp examination is negative, and direct cultural examinations of the hairs and skin demonstrate no fungi. The remainder of the laboratory and physical examinations are normal.

Histologic examination of the lesion on the nape of the neck revealed the following findings: "The epidermis is moderately acanthotic and shows intercellular edema. The latter is more pronounced in the outer root sheaths of hair follicles and becomes extreme in the region of the sebaceous glands. These are transformed into myxomatous-looking tissue with stringy basophilic material between stellate epithelial cells. The lumen of the follicles is widened and contains keratinous material surrounding the hair. There is moderate cellular infiltrate of lymphocytes, large mononuclear cells and some eosinophils. The infiltrate surrounds hair follicles and is more pronounced in the subepidermal zone."

Treatment: Four weekly exposures of 75 r each of superficial x-ray to the lesion on the nape of the neck resulted in lessening of edema.

Discussion

DR. HERMANN PINKUS: Since the first publication of 6 cases last year we have learned of at least 11 or 12 cases in the United States. Two of these are Dr. Zackheim's case and this case here. We have heard from several other doctors in various parts of the country who have seen cases. One case was presented by Martin-Scott, in England, last December under the same diagnosis (*Proc. Roy. Soc. Med.* 51:322 [Dec.] 1957). I have seen the slide and it is definitely a similar case. Braun-Falco in Germany has published about the histochemistry of this disease (*Dermat. Wchnschr.* 136:1289, 1957). He has analyzed the nature of this mucin with various procedures. If you looked at the sections here today that were stained with Alcian blue and periodic acid Schiff (PAS), you noticed that PAS actually shows very little of this mucin but that most of it was stained brilliantly with Alcian blue. So it is acidic in character and in that respect resembles connective tissue mucins. In other respects, as pointed out by Braun-Falco, it resembles substances normally found in the cells of the outer root sheath. Braun-Falco identifies it with the acid glucoproteins of Blix and feels that these are substances which are liberated within the cells out of normal material, where they were bound to protein. He gave the process the name of mucophanerosis, that is the appearance of mucin rather than new formation of mucin. The mucin then apparently accumulates between the cells and in cystic spaces in the sebaceous gland and outer root sheath. The process may extend upward to the infundibulum, but the lower segment of the follicle often resists for a long time. The hair, meanwhile, gets loosened and eventually falls out. In many cases this is a reversible process. As the process heals, the hair can easily grow back again. X-ray treatment probably is curative if it temporarily destroys the affected epithelium, especially the sebaceous glands. If the life processes of the hair follicle are temporarily arrested, the pathological process subsides and the hair grows in again. Unfortunately, not all cases responded. The cause of the disease remains unknown. The very first case, described in 1939 by Lehner and Szodoray, in Budapest, was that of a young man with extensive lesions of this kind. He developed them in crops over several months, then cleared up and got well spontaneously without any treatment. Lehner and Szodoray called it follicular edema with mucin formation (*Dermat. Wchnschr.* 108:679, 1939). They wondered if it might be a virus infection. I have considered the same possibility and so has Braun-Falco, but we have no proof.

Porphyria Cutanea Tarda. Presented by DR. ISADORE BOTVINICK.

Porphyria Cutanea Tarda with Sclerodermalike Changes of the Upper Trunk. Presented by DR. EUGENE A. HAND.

Discussion

DR. STANLEY GREENBERG: The second patient has porphyria cutanea tarda with sclerodermoid changes of the anterior chest and back and flexural surfaces of the wrists rather than scleroderma with chance associated porphyria.

Both patients presented urines which fluoresced a pinkish color, indicating the presence of porphyrins; however, this finding alone is not of great significance, since porphyrinuria exists in a variety of conditions, as well as occasionally in normal persons.

We are obliged to determine the nature of the porphyrins excreted; namely, whether they are porphoblinogen or copra- or uroporphyria. Without these determinations, the history and clinical picture must be used to rule out other types of porphyria. Neither of these patients had symptomatology suggestive of the intermittent acute type, and certainly there is nothing to indicate the erythropoietic type.

I should like to make several suggestions. 1. Do liver-function studies on these patients. Porphyria represents a metabolic error and is frequently associated with liver damage. 2. Check other members of the family, for the trait is considered to be transmitted as a mendelian dominant. Urinary and

fecal studies have often revealed abnormal findings in persons having no clinical signs. 3. Alcohol is known to play a role in porphyria, and abstinence should be stressed in these patients who give history of drinking. 4. As far as treatment is concerned, most recently the chelating agents have been used, especially in the intermittent acute variety, with some success. Also, several cases of cutanea tarda which have been borderline intermittent acute have been reported improved. Another drug which has been used is chloroquine (Aralen). However, investigators differ in opinion: Some say it cures; others say it precipitates porphyria.

DR. PATRICK WILSON: Both these patients had fragile, brittle skins characterized by slowly healing superficial ulcerative lesions following minor trauma for a period of many years before development of the full-blown syndrome. I think it might be well to keep this preliminary change in mind as possible evidence of early porphyria in patients showing such changes.

DR. ARTHUR JAMES: The first patient told me that exposure to sunlight had no part in the production of lesions on his hands but that they came on after injury. When his hands were traumatized bullae appeared in the sites of trauma. I believe that he has epidermolysis bullosa.

DR. STANLEY GREENBERG: They do not necessarily develop their bullae on exposure to sunlight. In fact, it is usually hard to deliberately precipitate them on exposure to ultraviolet, but the bullae do appear after minor trauma in areas that have been exposed to sunlight.

DR. GEORGE SEXTON: Two years ago I reported such a case (*Canad. M. A. J.* 74:909-911, 1956) with a review of the literature. My case was a woman, 70 years of age, who had hypertrichosis melanosis, bullous lesions with easy trauma, photosensitivity, and vague abdominal symptoms. The increased growth of hair on the face was extensive, and she presented colored urine. This woman never took a drink of alcohol in her life and had never had any barbiturates given to her. Sulfobromophthalein (Bromsulphalein) was elevated, and although the blood and urine did not show any evidence of glycosuria, she did show an elevated glucose-tolerance test, all of which suggested liver damage. The only thing I could attribute this to was that she had had an infected thrombophlebitis in the lower leg, which might have been indirectly responsible for the damage to the liver. Appropos the use of chelating agents it is notable that Schrumpf (*Lancet* 2:1226, 1952) reported on the use of dimercaprol (BAL) with distinct benefit in a latent form of porphyria.

A Study of the Epidermal Clear Cells with Special Reference to Their Relationship to the Cells of Langerhans. Presented by DR. ROBERT J. SCHOENFELD.

The Absence of a Fungistatic Effect of Squalene on Dermatophytes. Presented by DR. H. S. ZACKHEIM and DR. BENJAMIN MIHAY.

Incontinentia Pigmenti. Pityriasis Rubra Pilaris. Pityriasis Lichenoides Chronica. Alopecia Areata. Scarring Alopecia (Folliculitis Decalvans? Lichen Planopilaris?). Lupus Tumidus (Vulgaris). Larva Migrans. Trichoepithelioma. Presented by DETROIT RECEIVING HOSPITAL.

Pyoderma Gangrenosum? Presented by DR. EUGENE A. HAND.

Case for Diagnosis: Chromoblastomycosis? Presented by DR. ALICE E. PALMER and DR. STANLEY GREENBERG.

Kaposi's Sarcoma. Presented by DR. A. P. WILSON.

Superficial Epitheliomatosis. Presented by DR. GEORGE G. SEXTON.

Pityriasis Rubra Pilaris. Presented by DR. FRED V. HAUSER.

Scleroderma. Presented by VETERANS ADMINISTRATION HOSPITAL, Dearborn, Mich.

METROPOLITAN DERMATOLOGICAL SOCIETY OF LOS ANGELES

Laurence J. Underwood, M.D., President
Eliot Wolk, M.D., Vice-President
Max Popper, M.D., Secretary

Oct. 28, 1958

Recurrent Sclerosing Basal-Cell Carcinoma.

Presented by DR. FLOYD J. DORNBUSH.

This 68-year-old white woman was first seen by me in 1953 because of a lesion on the left temple. At that time she stated that she had had a skin cancer which was treated with four x-ray treatments approximately six years previously. After these x-ray treatments, the entire lesion was excised. The wound never healed completely.

When first seen she presented a 2 in. long, linear scar, overlying the left eye with a central ulcer, 5×8 mm. in diameter. It was felt that this represented a recurrent basal-cell carcinoma. At that time, it was thoroughly curetted and desiccated in the Los Angeles County General Hospital. The lesion healed but did not remain free of disease. Six to eight months later, it began to scale and ulcerate again. At that time, the entire scar was excised in an oval, approximately 2 in. long, excision. The graft took well.

Submitted for publication Dec. 24, 1958.

However, in September, 1957, a relapse occurred with scaling and ulceration. The 3 in. long scar was excised, including the periosteum. The wound was left to granulate and subsequently healed.

However, in September of this year, she had a recurrence. A biopsy specimen was obtained which proved to be a typical basal-cell carcinoma. At the present time, this patient is considered a candidate for chemosurgical removal of the lesion.

Discussion

DR. STANTON MAY: I believe the only chance for a permanent cure is the use of chemosurgery, the Mohs' technique. About one year ago, I presented a similar case before this Society. Mohs' treatment was successfully performed. The lesion proved to be much more extensive than could have been suspected. While most cases will respond to conventional therapy, an occasional case will defy this treatment.

DR. JOHN B. WATSON: I should not recommend the Mohs' treatment. Electrosurgery, followed by x-ray therapy, would be preferable, because of less scarring and better cosmetic results. Mohs' treatment should be reserved for extensive and invasive epitheliomas.

DR. JAMES L. LYNCH: I believe that the lesion could be eradicated most successfully by a surgical approach. A plastic surgeon, employing frozen sections, could excise wider and wider, until points were reached around the whole circumference and depth where no more tumor cells could be found.

DR. CLETIS S. DORSEY: Dr. Pillsbury states in his textbook that a recurrent basal-cell carcinoma should not be treated by curettage and desiccation. Recurrence is an indication for surgical excision, preferably by a plastic surgeon. In the treatment of malignancies on the face, the plastic surgeon, employing multiple frozen sections at the time of surgery, can insure complete removal of the lesion, and the resulting scars are usually superior to those produced by any other form of treatment. However, even on the face, there are malignant lesions which are best treated by dermatologists.

DR. HAROLD C. FISHMAN: I am very strongly opposed to that point of view. Statistics show that recurrences occur much more frequently after surgical excision that after conventional dermatological treatment.

DR. MURRAY ZIMMERMAN: I agree with Dr. Fishman. We can treat these tumors better than surgeons, because we know the tumor better.

DR. LEONARD E. SAVITT: In a few similar cases, I performed (prior to treatment) about eight biopsies around the periphery of the lesion, marking the location of each. This procedure gave me the desired information about the probable extent of the lesion.

DR. ELIOT WOLK: There are cases (and this is one) where a plastic surgeon can completely eradicate the tumor. In such a case, he would perform a wide excision and await a report of the frozen section. Further surgery would be performed if the report indicated tumor cells at the margins. Furthermore, fairly good cosmetic results can be expected from an expert plastic closure. I believe, therefore, that we should admit the superiority of this procedure when we are faced with difficult problems such as this, in cases which may not be cured with conventional dermatological therapy.

DR. ANITA GELBER: This patient presents a problem in therapy because of her age (68 years) and the character and size of the lesion. The involved area is about 2×3 in. in size, consisting of radio dermatitis (due to previous x-ray therapy) and a large contracted scar with some activity at its border. I believe it is advisable to treat a patient with this type of lesion, and in this age group, as follows: (1) treatment of each lesion as it appears and (2) wide surgical removal of the involved area with subsequent plastic repair. In my opinion, this patient is not suited for Mohs' treatment.

DR. SIDNEY J. ROSE: This case meets the requirements of employing chemosurgery. If dermatologists were readily available to perform Mohs' technique, I do not think there would be any question about our decision in this case.

DR. VINCENT P. BURBY: I agree with Dr. Rose. It would be very desirable to include the performance of Mohs' technique in the training of dermatologists.

Congenital Ichthyosiform Erythroderma. Presented by DR. JACK KRAMER.

Chronic Recurrent Cheilitis (Solare?). Presented by DR. LAURENCE J. UNDERWOOD and DR. WALTER S. GREEN.

Generalized Psoriasis after Termination of Triamcinolone. Presented by DR. WILLIAM B. REED.

Incontinentia Pigmenti. Presented by DR. ROSE B. SAPERSTEIN.

Recurrent Sclerosing Basal-Cell Carcinoma. Presented by DR. FLOYD J. DORNBUSH.

Erythema Streptogenes Vs. Atypical Lupus Erythematosus. Presented by DR. MURRAY ZIMMERMAN.

Cavernous Hemangioma of Eyelids. Presented by DR. STANTON B. MAY, for management suggestions.

Onycholysis (Psoriasis of Nails?). Presented by DR. STUART H. MARTEL.

Koilonychia (Spoon Nails). Presented by DR. ROSE B. SAPERSTEIN.

Probable Discoid Lupus Erythematosus, Resistant to Therapy. Presented by DR. STANTON B. MAY, for discussion of management.

Treatment-Resistant Psoriasis. Presented by DR. STANTON B. MAY, for therapy suggestions.

NEW YORK DERMATOLOGICAL SOCIETY

J. Lowry Miller, M.D., President
Frank E. Cormia, M.D., Secretary

May 27, 1958

Hemangioendothelioma of the Floor of the Mouth in an Identical Twin. Presented by Dr. Maurice J. Costello.

An identical twin boy aged 22 months was first seen three days ago. He presents a hemangioendothelioma on the floor of the mouth measuring about 5.5 cm. by 1.25 cm. by 1.25 cm. It is large enough to cause protrusion of the tongue about 2 cm. When palpated it has a solid consistency, with a regular, smooth surface about the color of the oral cavity. It is not painful, ulcerated, or nodular, but it causes increased salivation. It interferes mechanically with chewing and swallowing.

The child weighs 19.5 lb., which is 4 lb. lighter than his identical twin, who does not have a similar lesion. His weight was 1 lb. less at birth. His height is 32¾ in.

About two months after the birth of this infant on July 15, 1956, a tumor was seen on the right side of the floor of the mouth under the tongue. At that time it was thought by his physicians to be a cavernous hemangioma. When he was 7 months old an attempt was made to excise the growth, but the operation could not be continued because of the condition of the infant. However, tissue was obtained for histologic study, and a diagnosis of "benign hemangioendothelioma of the infantile type" was made by the pathologist. About three months later surgical excision was again advised by two surgeons, one in New York City and the other in Philadelphia. The parents did not accept the advice because of the critical condition of the infant after the first operation. A radiologist in Philadelphia was consulted on Oct. 19, 1957, when the child was 15 months old.

On Nov. 12, 1957, the radiologist inserted 7 radon seeds of 0.1 mc. each into the soft tissues in the floor of the mouth and tongue. This was followed by a moderate reaction consisting of increased swelling in the irradiated area. The reaction subsided over the ensuing weeks. The tumor has not increased greatly in size since that time.

The parents did not think there was an appreciable decrease in the size of the tumor, but the radiologists based their impression of improvement on the fact that there was less swelling and the child's tongue no longer protruded beyond the vermilion margin. The radiologist saw the baby again on May 12, 1958, and recommended that the radon seed implantations be repeated, using the same dosage—7 tubes, each containing 0.1 mc.

Submitted for publication Oct. 11, 1958.

The opinion of the members on the following points would be appreciated:

1. Should roentgen rays be administered?
   (*a*) Is the tumor radiosensitive?
   (*b*) If indicated, how should irradiation be delivered?
   (*c*) Would there be sequelae—underdevelopment of the bones of the jaw, etc.?
   (*d*) Should radon seeds, radium, or x-rays be used?
2. Should the lesion be surgically excised?
   (*a*) Would it be successful, or might there be a lethal outcome?
   (*b*) Would it compromise speech, chewing, and swallowing?
   (*c*) Would there be a resultant deformity?
3. What are the possibilities of maligant degeneration if the lesion remains untreated? Might there be sudden obstruction? Will it recede with time?

Discussion

Dr. George M. Lewis: I feel a good deal as Dr. Machacek does, that ultimately surgery will be required. However, I think further irradiation might be tried, since the child has had a minimal dose, and if that caused improvement I see no reason why it could not be continued.

Dr. Carl T. Nelson: I should favor further and perhaps more enthusiastic implantation of the radon. If this is a hemangioendothelioma and not an ordinary hemangioma, I should expect it to be rather resistant to radiation.

Dr. Eugene F. Traub: I suppose the biopsy specimen was taken from the periphery. Part of this lesion seems to be a tumor, or at least there is considerable infiltration which we did not have an opportunity to palpate. At any rate, there is an element not radiosensitive. In small hemangiomas of the mouth small doses of irradiation will often initiate regression, but if they are fibrotic, or possibly some other type of tumor which may not have been picked up by the original biopsy, the question of surgical interference will have to be considered. If the lesion is not increasing in size or giving too much trouble—and there has apparently been some regression—it may be well to wait. In the case of the lesion on the upper lip in the child I brought from Philadelphia surgical removal was necessary, and there was considerable doubt as to the malignancy or benignancy of the tumor. The child got a fairly

good result and apparently so far is all right, but nothing but extensive surgery did any good. Even after extended histologic examination there was some difference of opinion regarding malignancy.

DR. MAURICE J. COSTELLO: Was that child given x-ray treatment? (Answer: Never.)

DR. GEORGE C. ANDREWS: The few cases of hemangioendothelioma that I have seen in infants have always been firmer when palpated and also more radioresistant than hemangiomas. They are usually curable by radiation, however. I believe that this child should continue treatment as outlined by Dr. Prendergass. The child is in good hands, and more treatment will probably reduce the lesion considerably. I should not say that operation may not be advisable eventually, but after the tumor has shrunken and the child is older operation would not be too difficult, whereas now it would be hazardous. As a child grows older, the mortality from operation becomes less and less. I think the present plan is the best one to follow for the time being. A similar case which I had under my care had to be operated on because the child could not breathe. He had received radiation by x-rays and by radium needles without benefit. The child lived, but it was a hazardous operation.

DR. MAURICE J. COSTELLO: Do you think the method used in this case to date—implantation of radon—should be continued? Do you think the dose was large enough?

DR. GEORGE C. ANDREWS: Yes, it is a very good method. Each cubic centimeter of tissue gets a tiny dose of fairly hard radiation. There is no injury to the bone from it.

DR. MAURICE J. COSTELLO: Do you think the dose was large enough?

DR. GEORGE C. ANDREWS: Of course a larger dose would be more effective. He may double the dose or use the same dose again. Either would be all right, in my opinion. He is being conservative.

DR. DOUGLAS TORRE: I think the patient will come to surgery sooner or later. The question is whether the first irradiation has done much good. Even without resolution of the tumor, it would grow relatively smaller as the child grows. There does not seem to be any permanent damage to the deep tissue. I should advocate waiting for surgery until the child is older.

DR. ANTHONY C. CIPOLLARO: This child is apparently in good general health. I believe the response to radiation would have been more satisfactory if it had been applied soon after the lesion made its appearance, and in larger dosage. The larger dose of radiation would produce some reaction, though not a severe one—probably some stomatitis—but it would probably not interfere with normal dentition. If the lesion does not disappear after another treatment or two, it would be necessary to resort to surgery.

DR. JOHN C. GRAHAM: I am not in favor of doing too much to the child at present. One more radiation in moderation might be indicated, but this lesion is apparently not growing, and there may be some absorption of this tumor mass. I am not in favor of anything radical. I believe surgery eventually will be necessary, but it would be better to put it off for several years.

DR. MAURICE J. COSTELLO: I was under the impression that these tumors were relatively radioinsensitive. The child was brought to me because he cannot masticate his food and is therefore losing weight. He is afraid to swallow his food for fear of choking. It is my intention to advise the parents of this child to return to Dr. Prendergass for further radon treatment.

Keratosis Pilaris. Presented by DR. FRANK C. COMBES.

Lymphoblastoma. Presented by DR. FRANK C. COMBES.

Florid Papillomatosis of the Nipple. Presented by DR. ORLANDO CANIZARES.

A Case for Diagnosis (Mycosis Fungoides?) Presented by DR. ANTHONY N. DOMONKOS.

A Case for Diagnosis (Fixed Drug Eruption? Melanosis?). Presented by DR. FRANK E. CORMIA.

Reticulum-Cell Sarcoma. Presented by DR. CARL T. NELSON.

Lichen Planus of the Mouth. Presented by DR. DOUGLAS TORRE.

Balanitis Xerotica Obliterans. Presented by DR. FRANK C. COMBES.

Necrobiosis Lipoidica Diabeticorum in a Man. Presented by DR. FRANK C. COMBES.

PHILADELPHIA DERMATOLOGICAL SOCIETY

James M. Flood, M.D., Chairman
Herbert A. Luscombe, M.D., Secretary

May 16, 1958

Foreign Body Reaction? Possibly to Silica. Presented by CAPT. JAMES H. LOCKWOOD (MC), U. S. N.

A white man, aged 28, presented in tattoos of the right forearm and right deltoid area brownish papular lesions confined to areas of brown shading. These lesions were moderately firm and nontender and exhibited no surrounding inflammation. Other tattoos showed no abnormalities. About 10 years ago, while in Norfolk, Va., the patient received a tattoo of the right deltoid area. About seven months

Submitted for publication July 14, 1958.

later his right forearm was tattooed in the same establishment. Since then he has had many other tattoos with no untoward response until about two weeks ago. Two weeks ago he noted development of papules in the brown areas of the tattoos on the deltoid area and on the forearm. The lesions were only mildly pruritic. A punch biopsy was performed on May 8, 1958. The biopsy site became infected, causing him to be admitted to hospital on May 14, 1958.

The patient recently started desensitization for allergic rhinitis. He had infectious hepatitis in 1949. He has had a fracture of the left arm. There is no history of cutaneous or pulmonary diseases.

The patient's medical examination was negative.

A urinalysis was normal. Blood studies revealed 14.8 gm. hemoglobin, 17,900 leukocytes, 71% neutrophils, 29% lymphocytes. A roentgenogram of the chest was within normal limits.

The report on the biopsy specimen taken on May 8 was "granuloma with sarcoid reaction."

Because of cellulitis at the biopsy site, the patient has been treated with oxytetracycline (Terramycin), 250 mg. by mouth, four times a day, and warm wet compresses.

Discussion

CAPT. JAMES H. LOCKWOOD: The interesting feature is that all of these papules and nodules have developed in brown areas. This is the first time, to my knowledge, that lesions have developed solely in brown pigmented tatoos. The pigment used to produce brown in tatoos is ochre and usually ferrous salts associated with silica and aluminum, and we wondered whether this might not be a silica granuloma developing in the brown areas. These have occurred only on the right arm. He has no brown areas in any other place.

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I wonder whether we can rule out a factitial condition. Once his attention was focused on the development of a couple of early lesions in the brown areas, then other lesions developed on the sites of brown tattoos.

CAPT. JAMES H. LOCKWOOD: This apparently developed spontaneously; he has had no concern about the tattoos; he had them put on as a very young sailor, 10 years ago, at the age of 18. None of the lesions have healed. They are still present and histologically were reported as granuloma with sarcoid-like reaction.

Scleroderma, Generalized. Presented by CAPT. JAMES H. LOCKWOOD (MC), U. S. N.

A white man aged 19, whose general health has been good, though he remembers tightness of the skin as a child, has universal tightness and firmness of the skin, least marked over the hands, feet, and genitalia. There is limitation of motion of all joints because of the taut skin. The skin is tender to firm palpation. The patient showed residual pigmentation about the face at the site of a flash burn, for which he was hospitalized on March 13, 1958. This responded well to treatment.

The tightness of the skin was severe enough during his teens to prevent strenuous activity, including sports. There was a spontaneous partial remission approximately a year ago, enough to permit his being taken into the Army and nearly completing his basic training when the burn occurred. Since entering the Army his cutaneous problem has become worse. The hands and feet have never been functionally involved.

A complete blood cell count and an electrocardiogram were within normal limits. The sedimentation rate was 16 mm. in an hour. A urinalysis was within normal limits. The total protein was 6.6 gm. %; albumin, 4.25 gm. %; globulin, 2.25 gm. %. Alkaline phosphatase, 4.5 Bodanski units; serum calcium, 10.1 mg. %. Liver-function studies gave normal results. Roentgenograms of the hands, feet, and chest were negative; studies of the gastrointestinal tract were negative; barium swallow was negative.

The report on the biopsy specimen was "compatible with scleroderma."

The patient has been treated with 250 mg. of chloroquine twice a day, with no response after four weeks.

Discussion

DR. MEYER L. NIEDELMAN: I recently had occasion to treat two patients with severe scleroderma with a drug recently reported upon by Dr. J. Rukavina (Rukavina, J. G.; Mendelson, C.; Price, J. M.; Brown, R. R.; and Johnson, S. A. M.: Scleroderma [Acrosclerosis] Treatment of 3 Cases of the Non-Calcific Variety by Chelation [EDTA], *J. Invest. Dermat.* 29:273-288, 1957). It is prepared and is sent to me by Abbott Laboratories. The drug is disodium ethylenediaminetetraacetic acid. This is a chelating agent and removes weak or unwanted metals by a mechanism of cation exchange.

This drug diminishes tightness and induration, reduces joint pain, and aids in the rate of ulcer healing. The daily dose for adults is 50 mg. per kilogram, with a maximum dose of 5 gm. dissolved in 500 cc. of 5% dextrose in water or isotonic saline. The solution is given intravenously very slowly over a four-hour period. The drug is given daily for five days and withheld for two days; this cycle is repeated three times. After several weeks the course may be repeated. Those who intend to use the drug should be acquainted with its reactions, although I have had no untoward complications. Both of my patients have had two

courses, with marked improvement in one patient and less in the other. I believe that this drug should be explored further for its possibilities. Perhaps the pathogenesis of scleroderma is related to metal-binding anomalies.

CAPT. JAMES H. LOCKWOOD: One of the interesting features is that this patient has had scleroderma since the age of 16; it has waxed and waned, and he was able to get into the Air Force with scleroderma without its being discovered.

Nodular Urticaria Pigmentosa. Presented by DR. CARROLL F. BURGOON JR.

Discoid Lupus Erythematosus in a Child. Presented by DR. CARROLL F. BURGOON JR. and DR. FREDERICK URBACH (by invitation).

Mycosis Fungoides. Presented by DR. ALFRED TROSOW.

Mycosis Fungoides. Presented by DR. CARROLL F. BURGOON JR.

Mucinoid Hair Follicle Disease (Pinkus). Presented by DR. CARROLL F. BURGOON JR.

Rheumatic Fever with Exanthem(?). Presented by DR. JOHN P. SCULLY.

Questionable Generalized Lichen Planus(?) Photosensitization Dermatitis(?) Dermatitis Medicamentosa(?). Presented by DR. JOHN M. SIEGEL.

Acne Rosacea. Presented by DR. CARROLL F. BURGOON JR. and DR. FREDERICK URBACH (by invitation).

Hair Loss, Dystrophy of the Nails, Apparently Systemic in Origin: Case for Diagnosis. Presented by DR. JOHN P. SCULLY and DR. IRVING IMBER (by invitation).

Lichen Sclerosus et Atrophicus. Presented by DR. JOHN P. SCULLY.

Maduromycosis (Organism Not Identified). Presented by CAPT. JAMES H. LOCKWOOD (MC), U. S. N.

Purpuric Eruption—for Classification. Presented by DR. CARROLL F. BURGOON JR. and DR. FREDERICK URBACH (by invitation).

Fox-Fordyce Disease. Presented by DR. LESLIE NICHOLAS and DR. R. A. HEISING (by invitation).

Secondary Syphilis. Presented by DR. DOROTHY LYNN.

Elephantiasis—Cause Undetermined. Presented by DR. LESLIE NICHOLAS.

A Case for Diagnosis. Presented by DR. LOUIS JAFFE and DR. M. M. GRATZ (by invitation).

PHILADELPHIA DERMATOLOGICAL SOCIETY

Herman Beerman, M.D., Chairman

Herbert A. Luscombe, M.D., Secretary

Oct. 17, 1958

Lichen Planus Circumfollicularis Corneus Comedoniformis (Kissmeyer).

Presented by CAPT. JAMES H. LOCKWOOD (MC), U. S. N.

A white man, aged 38, well developed and well nourished and in no distress, presented circular areas of alopecia on the trunk and extremities with 1 to 3 mm. firm papules around the periphery. Some of the papules had a yellowish color, with capillaries surrounding and converging toward the summit of the lesion. There were no papules in the central area of alopecia. There were numerous large comedones on the back and several yellowish periorbital, milia-like lesions. The condition had its onset nine years ago, with tender "folding" of the skin of both soles, with erythema and scaling, followed in one year with alopecia of the nuchal area and later circular areas of alopecia on the trunk and extremities. The only symptom was a mild pruritus.

The patient had the usual childhood diseases, also diphtheria. He had an appendectomy in 1950. In 1949 he was in an automobile accident, with possible trauma to the kidney.

The VDRL was nonreactive; a complete blood cell count and a urinalysis were within normal limits. A Roentgenogram of the chest was negative.

The report on the biopsy specimen was lichen planopilaris.

Submitted for publication Nov. 24, 1958.

The patient has been treated with chloroquine, 250 mg. b. i. d. for 12 days, then 250 mg. daily for the past three months, with very gradual improvement and clearing of the lesions on the soles.

Discussion

CAPT. JAMES H. LOCKWOOD: We were at a loss for a diagnosis in this case. There is a rather unusual topography of the lesions, circular arrangement with alopecia and comedones. We considered a number of possibilities, including Kyrle's disease. Clinically this did not fit well. We also considered alopecia mucinosa and did special stains for follicular degeneration. This did not fit. Looking through the photographs of a publication of the Ninth International Congress of Dermatology, in Budapest, in 1935, we found a picture and a description of a case somewhat resembling this, called by the name we have put on the protocol. That patient was a man about 60 who had lesions which were similar to these, in a circular arrangement on the trunk and extremities. We have no other diagnosis, unless this is a rare systematized nevus comedonicus. It is the only case like this that I have even seen. Should anyone have another diagnosis, we would welcome it.

DR. JOHN F. WILSON: I do not think one can pass by without mentioning that several features of this case clinically suggest the diagnosis of chloracne, primarily because of the comedones

and the location. Dr. Beerman, however, demonstrated one area of very sharply marginated infiltrate in one portion of the slide, and I wondered why this is not simply called lichen planopilaris.

DR. HERMAN BEERMAN: That is precisely what we called it histologically.

DR. GEORGE W. HAMBRICK JR.: I hope that Dr. Lockwood is willing to place a question mark in front of his presenting diagnosis. There are several features present in this patient's eruption which suggest a diagnosis of hyperkeratosis follicularis et parafollicularis in cutem penetrans—Kyrle's disease. The predominant lesion is a comedo; these are arranged in plaques with circular or arcuate outline. There are several solitary pustules present on the trunk, arms, and buttocks. In several histological sections, in addition to the large comedones, there are masses of free keratin-like material within the dermis about which a foreign-body reaction is occurring; this is consistent with a more extensive process than lichen planopilaris.

DR. JOSEPH V. KLAUDER: If I had seen this case clinically, I should have missed the diagnosis. I would have proceeded to extract those comedones. I think the presenter deserves credit for suggesting a diagnosis for this unusual eruption. As to chloracne, I see no resemblance whatever.

DR. JOHN E. GERMAN: The lesions on the feet are difficult to correlate with those on the trunk and neck, and the color of the lesions and the nationality of the man (Italian) tend to make me think of Kaposi's sarcoma. I think there are two different diagnoses here.

CAPT. JAMES H. LOCKWOOD: We thought that the lesions on the soles were different. There was no relationship histologically or clinically between the two lesions. The condition on the soles is much improved over what it has been for the past nine years, owing to chloroquine therapy. However, the lesions on the trunk have altered very little under this treatment.

Incontinentia Pigmenti. Presented by DR. HERBERT A. LUSCOMBE.

A white boy aged 8 weeks, in no acute distress, presented a slate-colored, speckled pigmentation of the upper arms and the sides of the trunk. On the left forearm and the left leg there were linear papular keratotic patches that simulated a linear nevus. On some of these patches were bullae 3 to 6 mm. in diameter. One such patch was present on the left sole. When first seen by the mother, the infant had blisters on the hands and feet which were treated with hexachlorophene (PhisoHex) baths. On the third day of life the boy developed tetany, which responded to calcium. Since then he has had recurring blisters on the hands and feet. In the past couple of weeks he has developed erythematous, keratotic-appearing patches on the left leg.

Discussion

DR. IRA L. SCHAMBERG: These lesions are much more extensive on one side than on the other. This is unusual in incontinentia pigmenti. The long linear process seen here I have not seen previously in incontinentia pigmenti. The early marbling and mottling on the trunk make the diagnosis indisputable.

DR. BERTRAM SHAFFER: I think it should be remarked that this is a boy and this disease is extremely rare in the male. I wonder if there is an eosinophilia, which is an important accompaniment of this condition in early infancy. Also I wondered if there was any fever, because when this disease begins in early infancy, fever is a symptom.

DR. ALBERT M. KLIGMAN: Are the long linear keratotic lesions a part of the incontinentia pigmenti or simply an associated ectodermal defect? People who study this disease say it is divided into two types.

DR. HERBERT A. LUSCOMBE: Three stages of incontinentia pigmenti have been described: an early bullous stage, a later papular or hyperkeratotic phase, and finally the classical pigmentation. This boy still shows evidence of all three stages. Haber (*Brit. M. J.* 1:104, 1949) reported a similar case. This child originally had fever and was thought to have impetigo. From previous experience with two cases, one of which showed the bullous and one only the pigmentary stage; I should say that the natural course of this disease is to spontaneous clearing—to go through the bullous stage, the papular stage, then the pigmentary, and then in a few years clear up. Frequently other ectodermal defects are associated, particularly those involving the central nervous system.

DR. JOHN P. SCULLY: Are there forms "fruste" of this condition? I saw a 7-year-old child in consultation the other day who had the spitting image of inactive incontinentia pigmenti, all on one side of the body, but there was no history of the previous bullous eruption. It had been present more or less since birth, that is, it certainly appeared in the first year, but there had been no evidence of bullae.

DR. ALBERT M. KLIGMAN: There is a type which goes through the phase you mention. Furthermore, this is not strictly an ectodermal disease. It is potentially a very serious disorder.

DR. THOMAS BUTTERWORTH: As with any other new disease, we hitch on a lot of other characteristics. I was very much interested a year or two ago in reading a quotation of a paper by a Japanese by the name of Ito, who described incontinentia pigmenti achromicans. (Quoted by

Kiamura, K., et al.: *A.M.A. Arch. Dermat. & Syph.* 69:671, 1954.)

DR. JACK WEINER: There is an excellent discussion of this delayed type apparent after infancy in the proceedings of the San Francisco meeting (A. M. A. ARCH. DERMAT. 77:144, 1958), which mentions a case in a child 2 years of age and one in another 5 years of age, manifesting these changes.

Erythema Figuratum Perstans. Presented by DR. HERBERT A. LUSCOMBE and DR. JOSEPH K. CORSON.

A white youth, aged 16, well nourished, in no distress, presented macular, scaling, erythematous patches, circular or arciform in outline, on the sides of the trunk primarily, with some rounded patches on the back, thighs, and legs. The patient was in good health until approximately eight years ago, when he began to notice scaling patches on the flexor surfaces of his forearms. These were mildly pruritic and would come and go. Approximately nine months ago, lesions occurred on the chest and spread to the back. The patient denies having had any of the childhood diseases. His only treatment to date has consisted of prescriptions for occasional "colds," for which the family doctor prescribed.

The patient's father, aged 49, is well, with no history of cutaneous disorders or other serious illnesses. The mother, aged 45, has been hospitalized for a nervous breakdown for the last four months. There is no other history of serious illnesses. There is no immediate family history of epilepsy, goiter, heart disease, peptic ulcers, allergic conditions, diabetes, or kidney disease.

The physical examination was within normal limits; examination of the head, eyes, ears, nose, throat, and mucous membranes within normal limits. No adenopathy or thyroid enlargement was noted. The chest was clear to auscultation and percussion, heart rate regular, no enlargement noted AP. Left thoracic sclerosis was present. The abdomen was soft, scaphoid. No masses, organs or tenderness was noted. No joint pathology was noted.

Complete blood studies revealed 14.0 gm. of hemoglobin, 9,750 leukocytes, 48% polymorphonuclear leukocytes, 43% lymphocytes, 8% monocytes, 1% eosinophils. Urinalysis was within normal limits. KOH scrapings were negative on three occasions.

The report on the biopsy specimen was "microvesicle of corneum with focal parakeratosis and light lymphocytic infiltrate of the dermis compatible with erythema multiforme."

The patient has been treated with resorcinol lotion locally, with some improvement.

Discussion

DR. JOHN P. SCULLY: I cannot agree with the diagnosis of erythema figuratum perstans here. There is too much of eczematoid reaction. I would say the diagnosis rests somewhere between nummular eczema, seborrheic eczema, or infectious eczematoid dermatitis. I do not think it belongs in the erythema group of diseases.

DR. IRA L. SCHAMBERG: Despite the three negative KOH examinations, I suggest a therapeutic trial with Whitfield's ointment.

DR. MEYER L. NIEDELMAN: I did not see any clinical evidence of erythema figuratum perstans, although the picture may have changed since Dr. Luscombe first saw the patient. I would favor a fungous infection and would do more scrapings and cultures. Certainly fungicides should be tried.

DR. ALBERT M. KLIGMAN: I favored a fungous infection, at first, but when I looked at is closely, I did not think so.

DR. GEORGE W. HAMBRICK JR.: The Kodachromes showing the eruption at an earlier time were excellent, and I believe support the presenter's diagnosis. One must consider that the natural evolution and involution of such eruptions often result in an eczematous appearance of the lesions. In addition, topical therapy, such as used on this case, would change the morphology of the lesions in this same direction. In some of these patients, administration of bismuth has caused a remission in the condition.

DR. REUBEN SCHWARTZ: This patient had quite a bit of seborrhea; there was a suggestion that it might be seborrheic dermatitis.

DR. HERBERT A. LUSCOMBE: As you can see by comparison of the patient with the Kodachromes taken two months ago, there has been a decided change in the clinical picture. One would expect change in this condition. Treatment, too, has altered the eruption, but the repeated absence of fungi on microscopic examination and on culture is certainly against the diagnosis of a fungus infection. The eruption most closely fits the description of erythema figuratum perstans, although I would rather call it erythema multiforme perstans.

Erythema Figuratum Perstans. Presented by DR. HERBERT A. LUSCOMBE and DR. HAROLD L. COLBURN.

Psoriasis. Presented by DR. HERMAN BEERMAN and DR. HERBERT S. LUSCOMBE.

Mycosis Fungoides. Presented by DR. HENRY B. DECKER and DR. HERBERT A. LUSCOMBE.

Hailey-Hailey Disease. Presented by DR. HERBERT A. LUSCOMBE and DR. HAROLD L. COLBURN.

Granuloma in Tatto. Presented by DR. HENRY B. DECKER and DR. HAROLD L. COLBURN.

Acne Conglobata with Hidradenitis Suppurativa (Electrosurgical Removal of Masses from Face and Ears). Presented by DR. HERBERT A. LUSCOMBE and DR. HERMAN BEERMAN and DR. GOPINATH (by invitation).

Parapsoriasis. Presented by DR. HAROLD L. COLBURN.

Parapsoriasis. Presented by DR. HERBERT A. LUSCOMBE.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

R. Raymond Allington, M.D., President
Ralph T. Behling, M.D., Secretary
Herbert L. Joseph, M.D., Editor

July 18, 1958

Pseudoxanthoma Elasticum. Presented by CAPT. DONALD G. MOYER (MC) A. U. S. (by invitation).

A white woman, aged 36 years, noticed the skin of her neck becoming loosened and thickened in 1949. Following minimal trauma to the right eye in 1952 there has been progressive loss of vision. For the past three years there have been dull aches and muscular cramps in the legs and during the past four months intermittent claudication in the right leg.

There are chamois-colored papules on the flexor surfaces of the extremities and on the neck. On the right retina is a macular scar, and there are bilateral angioid streaks. The peripheral pulses are generally decreased. X-ray films show calcification of the femoral arteries.

A slide from the skin biopsy shows the changes of pseudoxanthoma elasticum.

Discussion

DR. HAROLD M. SCHNEIDMAN: This disease is another instance of a condition once thought to be purely dermatologic but which, upon thorough investigation, has been shown to have visceral manifestations. The elastic tissue of the gastrointestinal tract and blood vessels as well as the retina and skin become involved.

We have been testing the circulation of a few patients with this disease and have found abnormal pulse waves. We feel this represents a disorder in the elastic tissue of the peripheral vessels. Some of our patients have had gastrointestinal hemorrhages, and one required repeated blood transfusions. It is suggested that all of these patients have gastrointestinal x-ray studies.

DR. HERBERT L. JOSEPH: I cannot recall a description of the histopathological changes in the eye. I should like to know if the changes in the elastic tissue in the eye are similar to those in the skin and vessels. It would be of interest to review the embryology of the elastic tissue in the eye and skin.

DR. GEORGE T. LENAHAN: This patient had full and bounding dorsalis pedis pulsations. Although she gives a history of intermittent claudication, the pain in the extremities does not disappear when she rests. This is difficult to interpret, especially with the adequate pulsations.

Submitted for publication Aug. 28, 1958.

DR. JAMES P. MCGINLEY: This is a hereditary disease. I have seen two cases where siblings had the condition. An article in an Italian journal reported 200 cases appearing in 60 families. Some of these cases showed only angioid streaks or symptoms referable to one organ system alone. Angioid streaks are lines of degeneration in Bruch's membrane.

DR. MANUEL F. ALLENDE: Angioid streaks are seen not only in pseudoxanthoma elasticum but also in Paget's disease of the bone. They are due to the defect in Bruch's membrane, which Dr. McGinley mentioned. Many of these patients have hypertension.

DR. MAX R. GREENLEE (by invitation): We have been following several patients with this disease in our eye clinic for about a year and a half. Since it has been mentioned in the literature that vitamin E is of value, we have been treating these patients with this preparation. In none have we seen improvement. We also have found that if patients have typical angioid streaks, a biopsy specimen of apparently uninvolved, normal-appearing skin shows the microscopic changes of pseudoxanthoma elasticum.

CAPT. DONALD G. MOYER (by invitation): There is elastic tissue destruction of the entire body in this disease. In addition to the angioid striae there is a marked tendency for retinal hemorrhage from minimal trauma. This patient's retinal hemorrhage followed splashing soap in the right eye, after which she worked very hard to cleanse the eye. Now there is no central vision on the right.

The angioid striae are splits of the internal elastic membrane of the choroid and the color is the imposition of the pigment of the retina on the pigment of the choroid. Inasmuch as choroids are pigmented differently depending on body color, angioid striae will be different colors. They can vary from a very light color to almost black. In this patient they are a rusty color.

As mentioned, hypertension occurs with pseudoxanthoma elasticum. Approximately one-half of the patients with this disease have hypertension, and some have died from malignant hypertension.

In this patient, the intermittent claudication stops when she rests, but the burning and cramping is almost continuous. The dorsalis pedis and anterior tibial pulses vary. Of the many times I have examined her, this is the first time I could feel these pulses, and tonight they were bounding. The

fact that she has been drinking this afternoon may have something to do with it. The radial pulses this evening are almost impossible to feel.

Upper gastrointestinal hemorrhage has been reported in 15 cases in the literature (*Gastroenterology* 31:2, 156-168 [Aug.] 1956). One had massive hemorrhage from the stomach, and at surgery bleeding was found from multiple areas. Another patient was described as having gastric and uterine hemorrhage and at autopsy showed destruction of the elastic tissue of all major abdominal vessels.

Vogt-Koyanagi Syndrome. Presented by Dr. Harold M. Schneidman and Dr. Thomas J. Sullivan (by invitation).

A 51-year-old Chinese man suffered sudden bilateral loss of vision in September, 1952. A few months later he noted falling hair and loss of hearing.

On examination of the eyes there is bilateral, severe anterior and posterior uveitis with retinal detachments. The hair is white to gray, sparse, and easily pulled out, with a patchy alopecia. Several large, irregular areas of depigmentation are on the face, neck, and upper extremities and smaller areas on the trunk. There is partial hearing loss.

Blood, urine, and radiological studies have all been normal.

He has received treatment with corticotropin (ACTH), cortisone, and cortisone drops to the eyes. A course of intravenous typhoid therapy was also given. In 1954 iridectomies were performed, and in May, 1957, the lens of the left eye was extracted for a cataract.

Since the onset of the disease the condition has remained essentially unchanged. At present he is able to see only hand movements at 4 to 5 ft. The skin remains unchanged.

Discussion

Dr. Rufus C. Rucker: This is the complete syndrome of Vogt-Koyanagi, including uveitis, alopecia, vitiligo, poliosis, and dysacousia. This is a rare condition and is probably seen more by ophthalmologists than by dermatologists.

Dr. David R. Taylor: I have heard the statement made that this is a virus disease. If so, it should have run its course by now. If the assumption that this is a virus is correct, continued maintenance therapy with steroids might be harmful. Have the steroids been stopped for a period of time to see if the condition improves?

Dr. Rees B. Rees: I believe this disease ultimately will prove to be one based upon genetic predisposition.

Dr. Edward J. Ringrose: Apparently Vogt-Koyanagi disease is very similar to Harada's disease. I discussed the disease with the ophthalmologists, and they do not believe the uveitis is viral in etiology; however, it is an inflammatory disorder.

Dr. Herbert L. Joseph: Two conditions have been presented in which the eye and the skin are involved, both of which may occur on an hereditary or genetic basis—pseudoxanthom elasticum and Vogt-Koyanagi syndrome. In both of these diseases there appears to be some essential congenital or developmental defect of ectodermal tissue. Further studies of the genetics and embryology of ectodermal structures may help our understanding of these and other congenital diseases.

Dr. Thomas J. Sullivan (by invitation): This patient is a classic example of Vogt-Koyanagi syndrome. Dermatologists first recognized this syndrome in the literature in 1948, whereas the ophthalmologists have written about it considerably since Vogt's first report, in 1906. In 1929, Koyanagi added the features of dysacousia and alopecia to Vogt's syndrome of uveitis, canities, and vitiligo. Harada's disease is identical with Vogt-Koyanagi syndrome, except that in Harada's disease the anterior uveal tract is spared.

This patient has been receiving steroids almost continuously since the onset of the disease, in 1952, but it has been stopped several times for three to four weeks. Each time there has been a definite decrease in visual acuity.

There have been only 60-odd cases of this reported in the literature, and six or seven have had changes in the spinal fluid with positive cell findings, indicating a viral etiology. Cultures never have been successful. Peters advanced the theory that this disease is caused by the destruction of the choroid pigment with dissemination of this throughout the body with sensitization of the various pigmentary structures of the eye, hair and skin.

Telangiectasia Macularis Eruptiva Perstans. Presented by Dr. Edward J. Ringrose.

A 35-year-old white male reporter complained of an intermittent eruption of approximately one year's duration. It began on the arms and spread to the chest and back. There has been no itching. At times the eruption becomes much more prominent.

At approximately the time the eruption began the patient was found to have a duodenal ulcer which has since responded to medical management.

The eruption consists of faintly violaceous small macules and maculopapules scattered over the upper extremities and trunk. They are more numerous on the upper extremities. Some of them are slightly brownish, suggesting urticaria pigmentosa. Urtication occurs promptly on irritation. The violaceous color disappears on diascopy, leaving a faint brown color. Stroking of the skin produces multiple small wheals along the path of

the stroke rather than true dermographism. Small wheals can be produced by rubbing the skin in uninvolved areas in addition to the involved areas.

The section shows dilatation of superficial blood vessels, a sparse perivascular round cell infiltrate and numerous mast cells in the upper cutis.

No treatment has been given.

Discussion

DR. RICHARD SKAHEN (by invitation): Some authorities believe this condition is synonymous with urticaria pigmentosa of adults. Mast cells are sparse in normal tissue, but, where found, they present several types of distribution. In the patient presented the mast cells have a definite perivascular distribution. This picture is not unlike that found in the tissues of humans and animals exposed to ionizing radiation. They may be in intimate relationship to small arterioles, especially in the lymph nodes. In urticaria pigmentosa they are found scattered in random fashion in the corium, with little morphological orientation relative to the blood vessels. This random scattering in the connective tissue is also true of the distribution of mast cells in the myxomatous ground substance of pretibial myxedema and in the edematous tissues of elephantiasis scroti. In these latter instances, the mast cells are associated with an "unglueing" of the connective tissue, for, indeed, this appears to be what takes place, allowing a collection of fluid between collagen fibers. There is also occasionally a collection of mast cells into discrete neoplastic nodules. This is found in humans and in dogs.

The pharmacology of the mast cell is enlarging. Its relationship to heparin, histamine, hyaluronic acid, and, more recently, serotonin have been investigated.

DR. REES B. REES: Telangiectasia macularis eruptiva perstans may be considered to be a variant of urticaria pigmentosa. Onset is in adult life.

DR. JOHN H. EPSTEIN: It would be of interest to do a bone survey on this patient.

DR. EDWARD J. RINGROSE: There is confusion due to the name of this disease, since there is no grossly visible telangiectasia. In the first case described, telangiectasia was present only over the nose. Histopathologically, however, there is dilatation of the terminal vessels, which produces the erythematous color. This also explains the fading on pressure.

In order to recognize the disorder it must be remembered that the clinical findings are minimal. The possibility of this diagnosis occurred to me when I palpated the patient's abdomen and urtication occurred on the skin in the palpated areas.

It is of interest that the original reported patient also had peptic ulcer. Increase in gastric hydrochloric acid secondary to the increased histamine in the tissues could explain this. The patient also has had headaches which might be from histamine. There is a possibility of histamine shock in patients with an overabundance of mast cells.

Lichen Sclerosus et Atrophicus. Presented by DR. MARTIN ASCH.

A 50-year-old, obese man first developed hard lesions on the upper back two years ago. This was followed by the appearance of white pruritic spots on the wrists, chest, and back. About the time of the onset the foreskin became irritated and circumcision was done. A few months later the glans became white. The white area has extended. The family doctor excised and electrodesiccated some of the lesions on the back and shoulders, but they recurred. Eighteen months ago severely itchy warty lesions developed over the right knee.

Numerous angular, flat, white maculopapular lesions are present over the wrists, chest, and back. On the right parietal scalp is a discrete firm lesion. There is a white macular discoloration about the urethral meatus on the glans penis. On the right knee there are hyperkeratotic verrucous plaques.

This slide shows marked hyperkeratosis and atrophy of the rete, with areas of liquefaction degeneration of the basal-cell layer. Some of the follicular ostia are dilated and filled with massive keratinous plugs. The upper corium shows marked edema with swelling of the collagen bundles and a peculiar felt-like appearance of the collagen. These changes occur in a band-like arrangement. Below this band of edematous connective tissue is an inflammatory infiltrate of round cells, occasional histiocytes, and plasma cells. The infiltrate is especially intense about the hair follicles and blood vessels.

Discussion

DR. REES B. REES: Chelating agents are now being used in the treatment of scleroderma with the thought that scleroderma may somehow be related to the presence of tract metals. Since lichen sclerosus et atrophicus in some instances resembles scleroderma, a trial treatment of this patient with chelating agents might be worth while.

DR. HERBERT L. JOSEPH: On the glans penis this disease sometimes is called balinitis xerotica obliterans and on the female genitalia kraurosis vulvae. While there is controversy about the matter, some cases of kraurosis vulvae apparently become squamous-cell carcinoma. This also can occur in balinitis xerotica obliterans but does so rarely. More frequently there is involvement of the urethra with a stricture or stenosis. Urological consultation is advised.

Case for Diagnosis: Collagen Disease? Epidermolysis Bullosa? Presented by DR. JOHN H. EPSTEIN and DR. FRANCIS J. SULLIVAN (by invitation).

Parapsoriasis en Plaque. Presented by DR. MARTIN ASCH.

Books

Practical Dermatology, Second edition. By George M. Lewis. Price, $8. Pp. 363, with 555 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5, 1959.

In this new edition, Lewis has managed to include a good deal of new material which brings the book up to date without greatly enlarging the size of the text. It is no small accomplishment, for, in addition to new sections on significant basic science developments, corticosteroids, dermabrasion, and tattooing, there is a large number of new illustrations for a total of some five hundred—all of them clear and well selected.

Designed primarily as a text for students and as a guide for practitioners, it follows the usual format with emphasis on history taking, physical examination, laboratory tests, and treatment, all of it written clearly, concisely, and without the distractions present in many encyclopedic texts. It is, in fact, as the title indicates, a practical, well-organized, uncomplicated introduction to dermatology.

Psychotherapeutic Drugs. By A. L. Welsh. Price, $4.75. Pp. 139. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1958.

The purpose of this book is to offer a brief but comprehensive survey of so-called tranquilizing drugs. Chemical formulas, pharmacologic actions, routes of administration and dosages, general indications, dermatological applications, and undesirable side-effects are discussed adequately but succinctly, and a lengthy reference list is included. The book will be welcomed by those desiring information about this group of drugs without the haze presented by the lay press and puffery groups.

Chloromycetin. No. 8. By Theodore E. Woodward and Charles L. Wisseman Jr.

Penicillin. No. 9. By Harold L. Hirsh and Lawrence E. Putnam.

Streptomycin and Dihydrostreptomycin. No. 10. By Louis Weinstein and N. Joel Ehrenkranz.

Modern Chemotherapy of Tuberculosis. No. 11. By Roger S. Mitchell and J. Carroll Bell. Antibiotics Monographs; $4 each. Medical Encyclopedia, Inc., 30 E. 60th St., New York 22, 1958.

This series of monographs provide reference works that are in the main excellent, practical, concise, and informative. The major portion in each book is devoted to the diseases in the therapy of which each of these drugs is useful. The disease pictures are described briefly, the causative organisms, their characteristics and vagaries are described, and then the treatment with the various drugs, with regard to specificity, dosage schedules, routes of administration, and side-effects.

Though the emphasis is on clinical aspects, sufficient attention is given also to phases such as the historical, pharmacology, susceptibility-testing, bacterial resistance, synergism with other antibiotic drugs, etc. Each of the books contains a well-selected list of reference works.

Although these books are not pointed toward them directly, dermatologists will find in them much that is predigested, interesting, useful, and current.

Melanoblasts and Melanocytes in Fetal Negro Skin. By Arnold A. Zimmerman and Samuel W. Becker Jr. Price, $2.25. Pp. 59, with 27 illustrations. University of Illinois Press, Urbana, Ill., 1959.

This monograph is an important contribution to our understanding of the nature and evolution of melanin-forming cells. Not only are past contributions reviewed and discussed, but the results of studies on one hundred six fetuses are presented. Excellent photographs of microscopic sections using special histochemical techniques, correlated with the age of the fetus, results in an easy-to-follow documentary of the development of melanoblasts and melanocytes. Evidence presented in support of the neural crest origin of these cells is convincing.

The book is highly recommended to both students and practitioners and, in particular, dermatologists.

Vascular Spiders and Related Lesions of the Skin. By William Bennett Bean. Price, not given. Pp. 372, with 130 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1958.

This is no ordinary book. It is neither a textbook nor a monograph, nor is it a collection of essays, yet in a sense it is all of these with a generous admixture of editorial comment and philosophical notes on the past, present, and future of medicine and is written in a delightful manner.

It seems that in his student days the author was discouraged and a little disillusioned that his teachers were unable to answer his questions about spider angiomas. His curiosity continued for twenty years, during which time he collected data about them; inevitably, in the course of the years new avenues for investigations were opened which soon led to studies of other vascular lesions, both related and unrelated to spiders, but all of them important because "no part of development, growth, normal function, disease, aging, or death is without its intimate vascular context."

This book is an account of these continuing studies which embraced in addition to vascular spiders, palmar erythema, Osler's disease, metastatic carcinoid, hemangiomas, telangiectases, livedo reticularis, glomus tumor, and a host of others. A few nonvascular conditions are included, such as fascial hernia, the nails in liver disease, and striate atrophy, only because they interest the author.

Dr. Bean, an internist, has on several occasions hurled gibes at dermatology for not going beyond the naming of an entity in Latin or Greek terms and describing its pathological picture; for being sunk by a naïve faith in nosology; for viewing medicine as something skin-deep, as an isolated problem, rather than as part of the bewildering complexity of man. No comment, other than to point out that internists who but recently discovered lupus erythematosus and scleroderma have not yet suggested more fitting names and that Dr. Bean coins such names as rubber-bleb nevi, venous lakes, cherry angioma, and caviar lesion.

But that is of little moment and may even serve a fruitful purpose, for the lesions with which this book is concerned do, in fact, except for isolated instances, get too little attention in dermatologic literature. Dr. Bean is faithful to his purpose, for he emphasizes ecology throughout the book, and his views are the result of innumerable observations, painstakingly documented, a thorough and critical review of the literature, an insatiable curiosity, and an infinite faith in the worth of clinical research.

Most of the book is given to a consideration of vascular spiders and palmar erythema discussed from every conceivable aspect—history, physiology, structure, clinical features, laboratory findings, mucosal lesions, relationship to liver disease, pregnancy and the normal state, etc., only therapy is not considered. Finally, there are some interesting and penetrating speculations on the mechanism with the statement that the observations of a humoral mechanism, i. e., estrogenic are on much firmer ground than the hypotheses.

The remainder of the book maintains the high pace although the diseases are not discussed as fully as are the sections on spiders. Throughout, there is an attempt to relate these various superficial and seemingly unimportant lesions to larger matters of great importance. There are nearly one thousand pertinent references, one hundred thirty illustrations, and a complete index. The final chapter is devoted to some philosophical thoughts on the current rise of the laboratory age in medicine and the decline of the personal side, and a plea is made for more and better clinical studies in a spirit of looking for, not just looking at.

Dr. Bean's book is outstanding in content, manner of presentation, in literary style, and as an example of the finest in clinical research and medical reporting. It is recommended highly for reading and rereading.

The Intragluteal Injection. By A. von Hochstetter, H. K. von Rechenberg, and R. Schmidt. Price, $1.15. Pp. 28, with 19 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart N, Germany, 1958.

Because of the occasional injury to nervous or vascular structures by the traditional technique of intragluteal injection, the authors advocate that the injections be administered into the lateral muscle group of gluteus medius and gluteus minimus, rather than the gluteus maximus. Excellent anatomical drawings and clinical photographs illustrate the rationale of the authors' thesis.

Occupational Tuberculosis of the Skin. By Fritz Kröber. Price, not given. Pp. 62. Editio Cantor, Aulendorf in Württemberg, Germany, 1958.

In central Europe, the morbidity rate of cutaneous tuberculosis is much greater than in the United States. Therefore, the question of the role of occupational trauma is not an uncommon problem. Covering the pertinent literature of the past twenty-seven years, the author has reviewed the various forms of exogenous and endogenous cutaneous tuberculosis as related to trauma and occupational hazards in general, including the transfer of the infectoin from animal to man. Although the discussion of the medicolegal aspects of the problem follows the concepts of German legislation, this monograph represents a valuable aid to anyone called upon to serve as a consultant in the field of occupational dermatology.

CORRECTION

The following footnote should have been included with the article entitled "The Pathogenesis of Superficial Fungous Infections in Cultured Human Skin" by Harvey Blank, M.D.; Seichiro Sagami, M.D.; Carolyn Boyd, M.S., and Frank J. Roth Jr., Ph.D., which appeared in the May issue of the ARCHIVES.

In a separate study we compared the ability of dermatophytes and nonpathogenic fungi to grow in a medium containing only keratinous material. A thick aqueous slurry was prepared of finely powdered plantar callus and added antibacterial antibiotics to control and prevent bacterial overgrowth. This medium was then inoculated with all of the common species of dermatophytes as well as 27 diverse species of saprophytic contaminant molds representing some 14 genera. All of the pathogenic forms and all except two of the saprophytic forms grew surprisingly well on this substrate. Sixteen of the saprophytic molds more luxuriantly and rapidly than did the dermatophytes. These observations indicate that keratinophilia or the possession of requisite enzymes for dissolution of epidermal keratin are not unusual or peculiar to the cutaneous pathogens. The restriction to an external nonviable host residence site cannot be explained by possession of a novel and characteristic enzyme mechanism by which dermatophytes alone can hydrolyze keratin.

because Neo-Polycin Ointment

helps clear topical infections promptly

Neo-Polycin® provides neomycin, bacitracin and polymyxin, three antibiotics preferred for topical use because this combination is effective against the *entire* range of bacteria causing most topical infections...has a low index of sensitivity...and averts the risk of sensitization to lifesaving antibiotics, since these agents are rarely used systemically. And Neo-Polycin provides these three antibiotics in the unique Fuzene® (polyethylene glycol diester) base, which releases higher antibiotic concentrations than is possible with grease-base ointments.

Each gram of Neo-Polycin contains 3 mg. of neomycin, 400 units of bacitracin and 8000 units of polymyxin B sulfate in the unique Fuzene base. Supplied in 15 Gm. tubes

PITMAN-MOORE COMPANY, DIVISION OF ALLIED LABORATORIES, INC., INDIANAPOLIS 6, INDIANA

ALCOHOLISM

an important problem in today's living!

The following articles from TODAY'S HEALTH are now available in one pamphlet for 50 cents . . .

ALCOHOLICS ANONYMOUS. Written from the standpoint of a member, the basic treatment procedures are described and the psychological problems confronting the alcoholic are discussed.

ALCOHOL AND CIRRHOSIS OF THE LIVER. Relationship between alcohol, diet and cirrhosis. Increasing stress on nutritional differences. by Russell S. Boles

HOW TO HELP A PROBLEM DRINKER. Understanding the alcoholic's capabilities, the necessity of help, causes of his condition. by Edward A. Strecker and Francis T. Chambers, Jr.

THE TREATMENT OF ALCOHOLISM. Tracing the steps from convincing the alcoholic that he is sick through treatment and cure. by Lewis Inman Sharp

CONDITIONED REFLEX TREATMENT OF CHRONIC ALCOHOLISM. Its place among methods of treatment today, its development and correlation with personality factors. by Walter L. Voegtlin

INSTITUTIONAL FACILITIES FOR THE TREATMENT OF ALCOHOLISM. Comparative differences, in drinking with the last century, new establishments and methods of treatment, lack of trained personnel. by E. H. L. Corwin

other pamphlets available . . .

ALCOHOLISM IS A DISEASE. A discussion by the Chairman of the A.M.A.'s Committee on Alcoholism. by Marvin A. Block, M.D., 8 pages, 15 cents

I AM THE WIDOW OF AN ALCOHOLIC. Three articles combined, by Virginia Conroy, 16 pages, 20 cents

HOW EXPERTS MEASURE DRUNKENNESS. A partial transcript of an actual courtroom case. by H. A. Heise, 8 pages, 15 cents

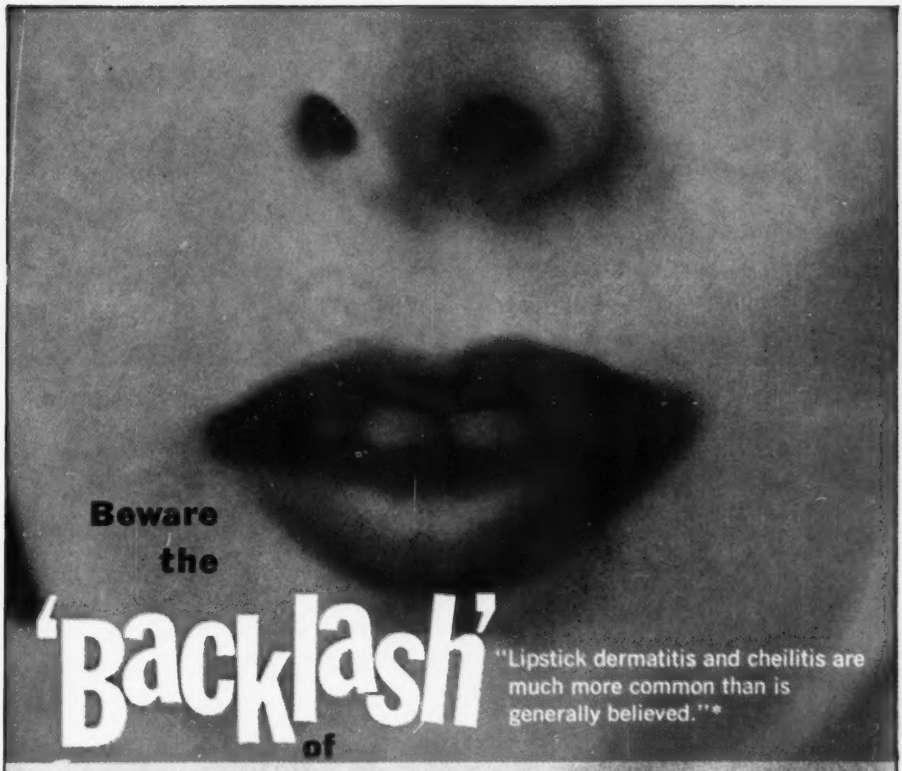
BARBITURATES, BOOZE AND OBITUARIES. A discussion of the dangers of mixing alcohol and barbiturates. by Donald A. Dukelow, 4 pages, 10 cents

TWELVE STEPS FOR ALCOHOLICS. A frank discussion of the meaning of an alcoholic behavior. by Richard Lake, 6 pages, 10 cents

address requests to . . .

ORDER DEPARTMENT

AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET, CHICAGO 10, ILLINOIS



Beware the

'Backlash' of Beauty

"Lipstick dermatitis and cheilitis are much more common than is generally believed."*

Dermatoses resulting from sensitivity to a variety of lipstick ingredients can be avoided by using MARCELLE Lipsticks — another reason to remember and suggest MARCELLE® HYPOALLERGENIC COSMETICS for the patient with a cosmetic allergy or sensitivity.

MARCELLE Lipsticks — available in a full range of colors — are offered in different formulas to eliminate common sensitizers, and to avoid perfumes and the bromofluoresceins. The MARCELLE Lipstick Testing Kit, providing 14 different formulations, enables you to help your patient select a lipstick best suited to her case.

Marcelle COSMETICS

Borden's PHARMACEUTICAL DIVISION
350 Madison Avenue, New York 17

Available in Canada through Prof. Sales Corp., Montreal

*Zakon, S. J., et al.: Arch. Dermat. & Syph. 56:499, 1947; abstracted in Birmingham, D. J., and Campbell, P. C., Jr.: Occupational and Related Dermatoses, U. S. Public Health Service Publication No. 364, 1954.

A PHYSIOLOGIC WET DRESSING FOR SKIN DISORDERS

PROPHYLLIN®

POWDER FOR WET DRESSINGS

PROPHYLLIN combines sodium propionate, a constituent of the protective secretion of normal skin, with water-soluble chlorophyllin. The result is a **natural,** nontoxic wet dressing, soothing in the most acutely inflamed skin disorders. It can be used even around the eyes and genitalia—or as a mouthwash—without fear of irritating the mucous membranes.

PHYSIOLOGIC: contains no chemical irritants or sensitizing agents

NONASTRINGENT: will not block sweat ducts

MARKEDLY ANTIPRURITIC

MILDLY BACTERIOSTATIC AND FUNGISTATIC

COSMETICALLY ACCEPTABLE: no staining, no objectionable odor

SUPPLIED:
In cartons of 12 packets. (Each packet contains 2.3 gm. of powder, for preparation of 8 fluid ounces of solution containing 1% sodium propionate and 0.0025% water-soluble chlorophyllin.) Also in 4-ounce and 16-ounce jars.

Rystan company MOUNT VERNON, NEW YORK

So many of the patients who open your door exhibit the common, non-inflammatory skin conditions in which steroids may be of little or no value.

SEBORRHEIC AFFECTIONS, especially of the scalp, such as "cradle cap" and dandruff

FUNGOUS INFECTIONS, including "athlete's foot," tinea capitis, etc.

SUBACUTE AND CHRONIC DERMATITIS where scaling and lichenification may be a problem

ECZEMATOUS ERUPTIONS following acute dermatoses of various etiologies

These are the candidates for the gentle keratolytic-bacteriostatic action of 'Pragmatar'.

PRAGMATAR®

an outstanding
tar-sulfur-salicylic acid ointment

SKF Smith Kline & French Laboratories

Never before in **ACNE!**

Graded long-term abrasion

The 3 grades of BRĀSIVOL permit a logical 3-step course of therapy:

1

Mild abrasion for 2-4 weeks with BRĀSIVOL FINE

2

More vigorous abrasion for 2-4 weeks with BRĀSIVOL MEDIUM

3

Maintenance treatment for as long as needed with BRĀSIVOL ROUGH

BRASIVOL introduces a new concept in the treatment of acne: prolonged superficial abrasion precisely adjustable to the patient's progress. Ten years of clinical studies in over a thousand acne patients have demonstrated the success of continuous abrasion in maintaining patency of the sebaceous ducts by gentle desquamation, thereby reducing comedones, papules, pustules and cysts, and minimizing post-acne scarring.

BRASIVOL contains non-silicon abrasives (fused synthetic aluminum oxide) of carefully selected particle sizes and in appropriate ratios, with hexachlorophene 1.0%, in a specially formulated base of soap and synthetic detergent.

1. Saperstein, R. B.: Presented at 107th annual meeting of American Medical Assn., San Francisco, Calif., June 23-27, 1958.

SUPPLIED:
Jars of Brāsivol Fine 6 oz.; Brāsivol Medium 6½ oz.; Brāsivol Rough 7 oz.

Brāsivol™

GRADED ABRASIVE CLEANSER FOR ACNE

Write for samples and informational literature

STIEFEL LABORATORIES, INC.
Oak Hill, New York

Canadian representatives:
WINLEY-MORRIS CO., LTD., Montreal 29, Quebec

FOUNDED 1847 STIEFEL®

In eczematous dermatitis with secondary infection CREME AND LOTION pH 5.0

COR-TAR-QUIN™

DOME

HYDROCORTISONE • STAINLESS TAR • DIIODOHYDROXYQUINOLINE
IN ALUMINUM ACETATE VEHICLE

COR-TAR-QUIN is especially effective in those dermatoses where an inflammatory reaction is accompanied by increased scaling, lichenification, and secondary infection.

Combined hydrocortisone-coal tar therapy produces an enhanced antipruritic, anti-inflammatory response and diiodohydroxyquinoline is fungicidal as well as bactericidal. The Acid Mantle creme base of COR-TAR-QUIN helps restore and maintain normal pH of the skin. Relief is prompt and lasting.

Sig: Apply b.i.d. ½ oz., 2 oz., and 4 oz. tubes with either 0.5% or 1.0% hydrocortisone

INCORPORATED IN EXCLUSIVE ACID MANTLE® VEHICLE

also available without the stainless tar, as CORT-QUIN™ CREME pH 4.5

A MOST TRUSTED NAME IN DERMATOLOGICALS

DOME CHEMICALS INC.

125 West End Avenue, New York 23, N. Y.
665 N. Robertson Blvd., Los Angeles 46, Cal.
2765 Bates Road, Montreal, Canada

10 SPECIALTY JOURNALS

PUBLISHED MONTHLY
BY THE AMERICAN MEDICAL ASSOCIATION

NEUROLOGY

GENERAL PSYCHIATRY

SURGERY

PATHOLOGY

DISEASES OF CHILDREN

OPHTHALMOLOGY

INDUSTRIAL HEALTH •

DERMATOLOGY

INTERNAL MEDICINE

OTOLARYNGOLOGY

Each journal offers the latest medical research and developments of outstanding specialists. Edited for the doctor by prominent authorities in each special field, these journals are of value not only to the specialist but to the general practitioner as well.

To order your subscription to one of the A.M.A.'s specialty journals use the form below..

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn • Chicago 10

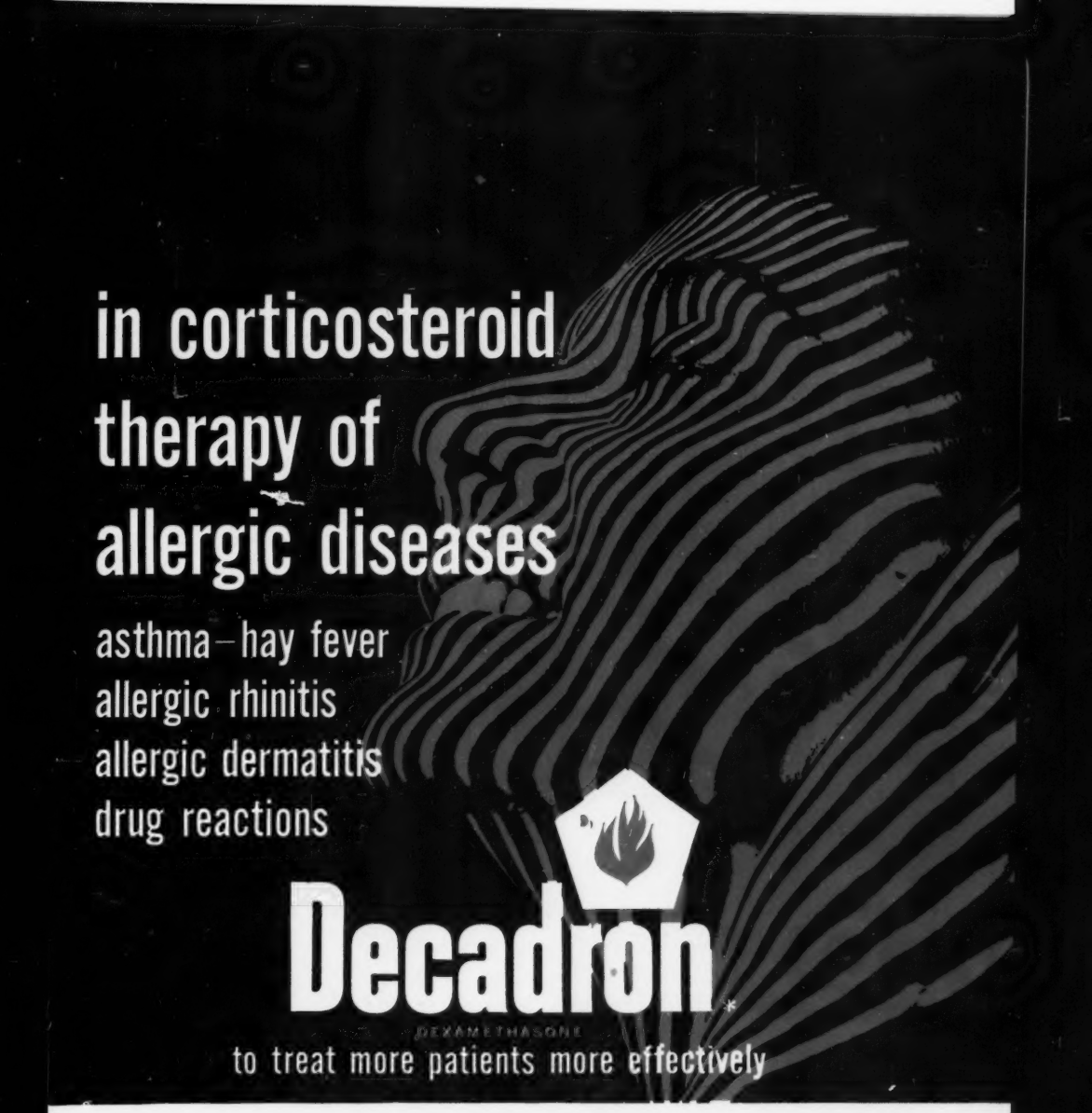
Please enter my subscription to the specialty journal checked at right.
Remittance for ☐ one year ☐ two years is enclosed.

NAME_____

ADDRESS_____

CITY_____ ZONE____ STATE_____

(One year rates)	U.S.A. & Possessions APO's	Canada	Outside U.S.A. & Possessions
☐ A.M.A. Arch. Neurology	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Gen. Psychiatry .	$14.00	$14.50	$15.50
☐ A.M.A. Arch. Dermatology....	12.00	12.50	13.50
☐ A.M.A. Arch. Industrial Health.	10.00	10.50	11.50
☐ A.M.A. Arch. Internal Medicine	10.00	10.50	11.50
☐ A.M.A. Jrl. Diseases of Children	12.00	12.50	13.50
☐ A.M.A. Arch. Surgery	14.00	14.50	15.50
☐ A.M.A. Arch. Pathology	10.00	10.50	11.50
☐ A.M.A. Arch. Ophthalmology..	12.00	12.50	13.50 •
☐ A.M.A. Arch. Otolaryngology..	14.00	14.50	15.50



a new order of magnitude

in anti-inflammatory potency in dosage reduction in avoidance of new side effects in therapeutic effectiveness in therapeutic range

Dosage: One 0.75 mg. tablet of DECADRON will usually replace one 4 mg. tablet of methylprednisolone or triamcinolone, one 5 mg. tablet of prednisone or prednisolone, one 20 mg. tablet of hydrocortisone, or one 25 mg. tablet of cortisone. Additional information on dosage and precautions is available to physicians on request.

Supplied: As 0.75 mg. and 0.5 mg. scored, pentagon-shaped tablets in bottles of 100 and 1000.

©1958 Merck & Co., Inc. *DECADRON is a trademark of Merck & Co., Inc.

MSD **MERCK SHARP & DOHME**
DIVISION OF MERCK & CO., Inc., PHILADELPHIA 1, PA.

SHEPARD'S
Cream Lotion

Contains sufficient sesame oil to lubricate without excess grease

Not occlusive

No lanolin or lanolin derivatives

Available unscented as well as scented

SHEPARD LABORATORIES
6615 N. CLARK ST., CHICAGO 26, ILL.

Manufacturers and Distributors of Fine Cosmetics

---

unexcelled

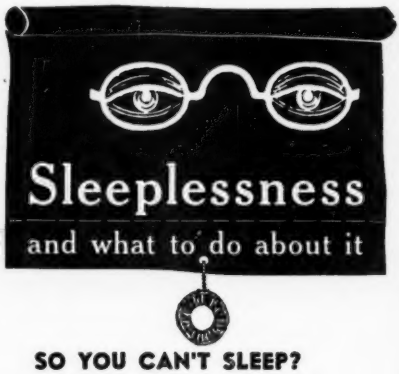
potentiation · efficacy · toleration

in broad-spectrum antibiotic therapy

COSA-TERRAMYCIN®
oxytetracycline with glucosamine

capsules	oral suspension	pediatric drops
125 mg. 250 mg.	peach flavored, 125 mg. per teaspoonful (5 cc.), 2 oz. bottle	peach flavored, 100 mg. per cc. (5 mg. per drop), 10 cc. bottle (with calibrated dropper)

Pfizer
Science for the world's well-being
PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, N. Y.



SO YOU CAN'T SLEEP?
by P. H. Fluck
8 pages, 15 cents

SLEEPLESSNESS AND WHAT TO DO ABOUT IT by Donald A. Laird, Ph.D.
8 pages, 15 cents

ROADS TO RELAXATION
by Joseph L. Fetterman, M.D.
4 pages, 10 cents

AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn St., Chicago 10, Illinois

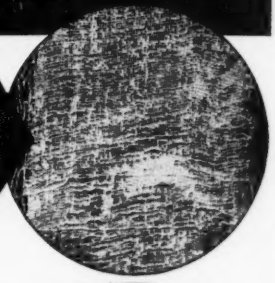
THE BEST IMPROVEMENT YET IN *UNNA'S BOOT*

NEW 4" x 10 YD.

Non-Ravelling

DOME-PASTE® BANDAGE

DOME

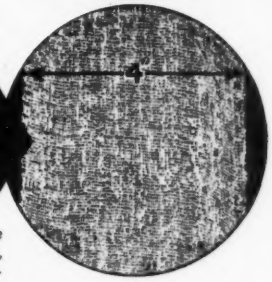


THE OLD

Frayed edges, uneven impregnation, difficult to apply.

•

Thread-locked edges, firmly woven; medicament spreads uniformly, easy to apply.



THE NEW

The new Dome-Paste bandage is flesh colored, 4" x 10 yd. gauze bandage... impregnated with glycerine, zinc oxide, gelatine paste.

RECOMMENDED

for leg ulcers resulting from thrombophlebitis (particularly the post partum and postoperative kinds), stasis edema and chronic venous insufficiency associated with varicose veins, and varicose eczema, lymphatic edema and thrombophlebitis of the superficial saphenous vessels.

AVAILABLE

individually wrapped in sealed polyethylene bags, inserted in metal cans to insure freshness.

DOME CHEMICALS INC.

125 West End Avenue, New York 23, N. Y.
665 N. Robertson Blvd., Los Angeles 46, Cal.
2765 Bates Road, Montreal, Canada

AN *Ethix* FORMULA

UNSCENTED

SHAMPOO

Myristic and lauric acids saponified with polyamine alkali to a low pH(8), with neutralized polycarboxylic acid, enriched with lanolin esters, given extraordinary solvency with propylene glycol.

Vegetable or mineral tars may be added in desired percentage.

Removes ointments and medications gently but thoroughly.

High foaming, extremely economical in use.

Tolerated by scalps which shed epithelium from overstrong detergents.

RETAIL PRICE $1.50 BOTTLE 6 OZ.

ETHIX CORPORATION
P. O. Box 115, Inwood 96, L. I., N. Y.
Send 1 oz. sample bottles of ETHIX FORMULA Shampoo to:
.....M.D.
.....
.....

A. M. A.
AMERICAN JOURNAL
OF
DISEASES OF
CHILDREN

integrate your knowledge—
subscribe to

A. M. A. Archives of
PATHOLOGY

A. M. A. Archives of
INTERNAL MEDICINE

A. M. A. Archives of
OPHTHALMOLOGY

A. M. A. Archives of
OTOLARYNGOLOGY

For a more complete reference shelf, we recommend these related journals. The variety of fields covered are especially appealing to the general practitioner with special interests. Each issue is important to your practice. Begin your subscriptions TODAY.

Department (D. C.)
AMERICAN MEDICAL ASSOCIATION
535 N. Dearborn St.
Chicago 10, Ill.

Begin my subscription(s) NOW, for:

A. M. A. .....

NAME .....

STREET .....

CITY .....STATE .....

integrate your knowledge by reading these related specialty journals . . .

A. M. A. Archives of INDUSTRIAL HEALTH

A. M. A. Archives of INTERNAL MEDICINE

A. M. A. Archives of DERMATOLOGY

Designed to save you hours of reading time through visual presentations . . . to provide you with timely tips every month . . . to place useful information at your finger tips, leaving less information on your reference shelf.

Write for subscriptions to:
AMERICAN MEDICAL ASSOCIATION
535 North Dearborn Street
Chicago 10, Ill.
Dept. (PATH.)

normal protective cover

Normal skin has an acid pH range between 4 and 6

Samples and literature on request

Supply:
ACID MANTLE Creme: 1 oz. tubes, 4 oz. & 16 oz. jars.
ACID MANTLE Lotion: 1 oz. and 4 oz. squeeze bottles, 1 pint bottles.

ACID MANTLE®

CREME or LOTION pH 4.2

In housewives' eczema and industrial dermatitis, promptly restores and maintains the normal protective acidity of the skin. Active ingredient is aluminum acetate in specially formulated bases.

"The importance of a measure designed to return the pH of the skin quickly to its normal values after exposure to soap and alkalies is amply borne out..."

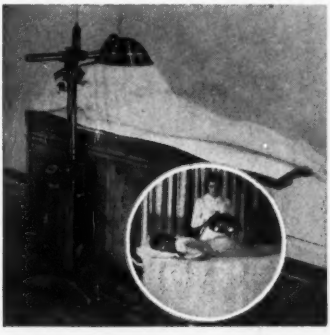
—Gross, P., et al.: A. M. A. Arch. Dermat. & Syph. 70:94,1954.

DOME CHEMICALS INC.

125 West End Avenue, New York 23, N. Y.
665 N. Robertson Blvd., Los Angeles 46, Cal.
2765 Bates Road, Montreal, Canada

A MUST IN DERMATOLOGY

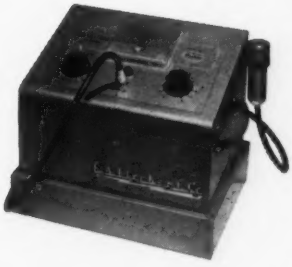
FISCHERQUARTZ



Model No. 88

A MUST IN DEPENDABLE

ULTRA SOUND



RF-7 Ultra Sound with new 6 or 12 foot very thin, flexible low volt cables.

R. A. FISCHER & CO.

FISCHERTHERM • FISCHERSINE • FISCHERQUARTZ • FISCHER ULTRA SOUND

**517-525 COMMERCIAL ST.
GLENDALE 3, CALIFORNIA**

A NEW WIDE-SPECTRUM TOPICAL MICROBICIDE

not an antibiotic... not a sulfonamide... not a nitrofuran

Triburon

Triburon-HC

(containing hydrocortisone 0.5%)

EFFECTIVE EVEN AGAINST ANTIBIOTIC-RESISTANT STRAINS

HIGHLY ACTIVE

■ against most "pathogenic cocci [both staphylococci and streptococci] regardless of their resistance to antibiotics."[1]

■ against pathogens common in skin and wound infections.

VIRTUALLY NONSENSITIZING

■ in more than 4500 stringent, closed-patch sensitivity tests, the incidence of allergic response was less than 2 per cent.[2, 3]

■ in initial clinical studies, only 15 of 1014 patients developed evidence of skin irritation.

MINIMAL RESISTANT ORGANISMS

■ laboratory attempts to develop Triburon-resistant strains produced no substantial change in organism sensitivity.[1]

■WIDE-SPECTRUM
■RAPID-ACTING
■WELL TOLERATED
■NONSTAINING
■ODORLESS

DIAGNOSIS AND NO. OF PATIENTS	DURATION OF TREATMENT	RESULTS	ADVERSE REACTIONS
Impetigo contagiosa (50)	Triburon 3-10 days	excellent	none
Ecthyma (24)	Triburon 5-14 days	excellent	none
Pustular folliculitis (16)	Triburon 1-3 weeks	infection controlled	3 complaints of burning
Dermatitis repens (18)	Triburon 1-2 weeks	infection controlled	none
Dermatitis repens (18)	Triburon-HC 1-4 weeks	excellent	none
Secondarily infected eczematous eruption (20)	Triburon 1-2 weeks	infection controlled	none
Secondarily infected eczematous eruption (64)	Triburon-HC 1-4 weeks	excellent	1 complaint of irritation

Chart based on finding of E. Edelson, E. Grunberg and T.V. Morton Jr.

PACKAGES:
Triburon Ointment, 1-oz tubes and 1-lb jars.
Triburon-HC Ointment, 5-Gm and 20-Gm tubes.

REFERENCES: 1. R. J. Schnitzer, E. Grunberg, W. F. DeLorenzo and R. E. Bagdon, to be published.
2. E. Edelson, E. Grunberg and T. V. Morton, Jr., **Antibiotics Annual 1958-1959, New York, Medical Encyclopedia, Inc., 1959.**
3. R. C. V. Robinson and L. E. Harmon, **Antibiotics Annual 1958-1959.**

TRIBURON™· triclobisonium chloride — N,N'-bis[1-methyl-3-(2,2,6-trimethylcyclohexyl) propyl]-N,-N'-dimethyl-1,6-hexanediamine bis (methochloride). ROCHE®

ROCHE LABORATORIES • Division of Hoffmann-La Roche Inc • Nutley 10 • New Jersey

UNEXCELLED PATIENT COMFORT and safety with DYCLONE™

dyclonine hydrochloride

an unsurpassed topical anesthetic

for
instrumentations
examinations
pain
pruritus

DYCLONE is a well tolerated topical anesthetic which is

fast-acting
long-acting
antibacterial
antifungal
virtually nonsensitizing

supply...Dyclone Creme, tubes of 1 oz. with rectal applicator. Dyclone Solution, bottles of 1 and 8 oz.

PITMAN-MOORE COMPANY
DIVISION OF ALLIED LABORATORIES, INC.
INDIANAPOLIS 6, INDIANA

Fostex® treats their acne while they wash

degreases the skin helps remove blackheads dries and peels the skin

...and this is how it works

Fostex provides essential actions necessary in treating acne. It washes off excess oil. It unblocks pores by penetrating and softening blackheads. It dries and peels the skin, removing papule coverings, thus permitting drainage of sebaceous glands.

Fostex contains Sebulytic®,* a combination of surface-active wetting agents with remarkable antiseborrheic, keratolytic and antibacterial actions . . . enhanced by sulfur 2%, salicylic acid 2%, hexachlorophene 1%.

*sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate and sodium dioctyl sulfosuccinate.

Your patients will like Fostex because it is so simple to use. They simply wash acne skin 2 to 4 times a day with Fostex, instead of using soap.

FOSTEX CREAM

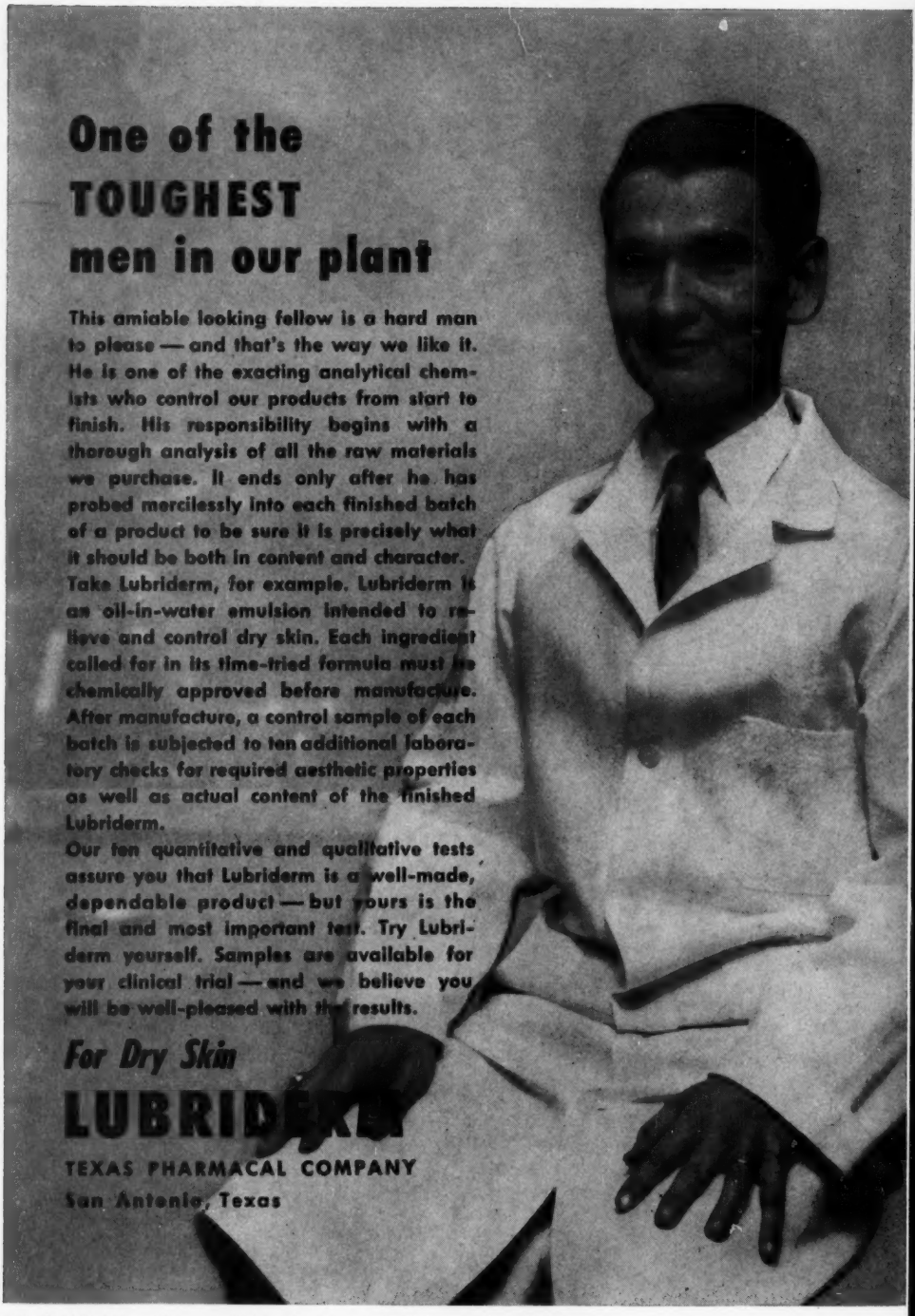
. . . in 4.5 oz. jars. For therapeutic washing in the initial phase of oily acne treatment.

FOSTEX CAKE

. . . in bar form. For therapeutic washing to keep the skin dry and free of blackheads during maintenance therapy. Also used in relatively less oily acne.

Write for samples.

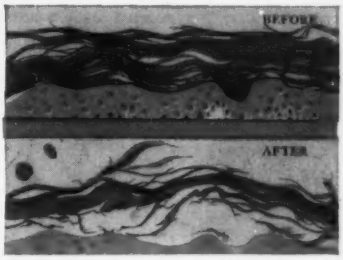
WESTWOOD PHARMACEUTICALS • **Buffalo 13, New York**


One of the
TOUGHEST
men in our plant
This amiable looking fellow is a hard man to please — and that's the way we like it. He is one of the exacting analytical chemists who control our products from start to finish. His responsibility begins with a thorough analysis of all the raw materials we purchase. It ends only after he has probed mercilessly into each finished batch of a product to be sure it is precisely what it should be both in content and character. Take Lubriderm, for example. Lubriderm is an oil-in-water emulsion intended to relieve and control dry skin. Each ingredient called for in its time-tried formula must be chemically approved before manufacture. After manufacture, a control sample of each batch is subjected to ten additional laboratory checks for required aesthetic properties as well as actual content of the finished Lubriderm.
Our ten quantitative and qualitative tests assure you that Lubriderm is a well-made, dependable product — but yours is the final and most important test. Try Lubriderm yourself. Samples are available for your clinical trial — and we believe you will be well-pleased with the results.
For Dry Skin
LUBRIDERM
TEXAS PHARMACAL COMPANY
San Antonio, Texas

IN CANADA—Omega Laboratories, Ltd., Montreal and Toronto
IN VENEZUELA—Salus, C. A., Caracas

New freedom from embarrassment and distress of psoriasis!

Alphosyl T.M. LOTION



DISAGGREGATES PSORIATIC SCALE

In vitro studies show that the keratin-dispersing action of allantoin is exceptionally effective in disaggregating psoriatic scale.[1,2] It apparently acts on an abnormal cement substance between cornified cells.[2,3] Coal tar, too, helps break up the horny layer.[2] Together, these agents provide rapid clearing of psoriatic lesions as well as the underlying inflammation and erythema.

ALPHOSYL Lotion, used by many physicians both in routine practice and in carefully controlled studies, proved highly successful.[2,4-7] The lotion permits complete avoidance of the potential hazards of certain other methods of treatment, such as superficial x-ray, heavy metals and corticosteroids.[7]

Advantages: • Treatment-fastness not observed • Cosmetic qualities permit free application to the scalp • Well tolerated • May be freely used on tender areas

FORMULA: Allantoin 2% and special coal tar extract 5% in a greaseless, stainless, vanishing lotion base.

SUPPLIED: Bottles of 8 fl. oz.

APPLICATION: For maximum therapeutic results rub thoroughly into lesions 2 to 4 times daily. For maintenance apply once or twice a week.

REFERENCES: 1. Flesch, P.: Proceedings Scientific Session. Toilet Goods Assoc. June, 1958. 2. Samitz, M. H.: Ann. New York Acad. Sc. 73:1020, 1958. 3. Flesch, P., and Jackson Esoda, E. G.: Ann. New York Acad. Sc. 73:989, 1958. 4. Bleiberg, J., and Saltzman, J. A.: Clin. Med. 5:485, 1958. 5. Bleiberg, J.: Ann. New York Acad. Sc.: 73:1028, 1958. 6. Clyman, S. G.: Ann. New York Acad. Sc. 73:1032, 1958. 7. Welsh, A. L., and Ede, M.: Ohio M. J.: to be published.

For psoriasis with acute inflammation

Alphosyl-HC T.M.

Alphosyl with 0.2% hydrocortisone
Supplied in bottles of 4 fl. oz.

R&C REED & CARNRICK
Jersey City 6, New Jersey

*TELES

Torch (available on prescription in 4 oz. bottles)

Really new, prompt and effective therapeutic agent in control of seborrheic dermatitis, itchy scalp and dandruff.

TELES * is a milk-white, unscented shampoo
TELES * may be employed at weekly intervals or less frequently
TELES * does not stain hair of any color
TELES * does not stimulate oiliness in the scalp
TELES * complete directions for use on each 4 oz. bottle

Samples and literature on request

Reference: Gross E. R. and Wright C. S., A. M. A. Archives of Dermatology, 78:92, July, 1958

TORCH LABORATORIES, INC.

110 Chestnut Street • Philadelphia 6 • Pa. *Tellurium Dioxide Suspension, Torch

NOW AVAILABLE

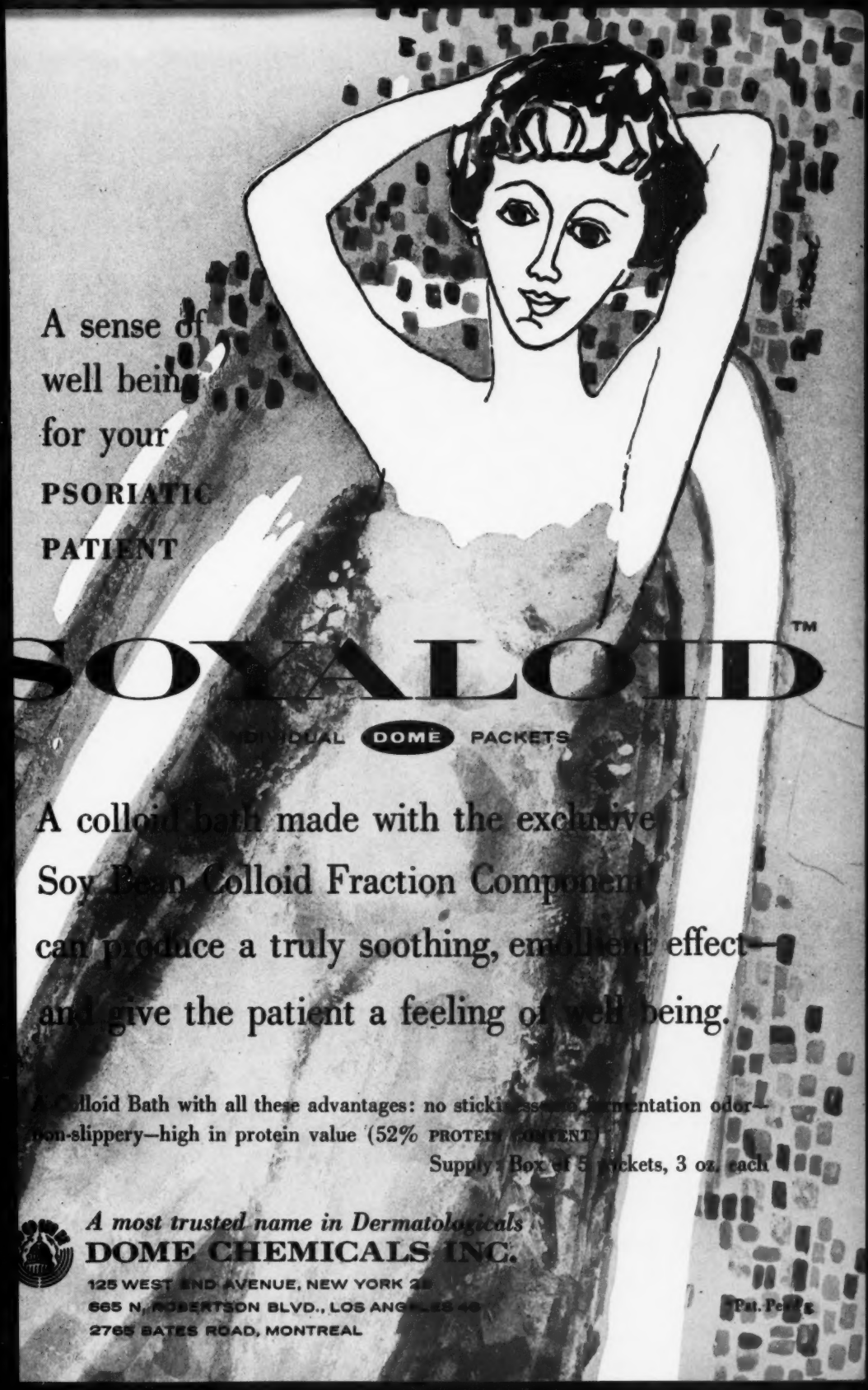
1958 EDITION

A.M.A. HEALTH PUBLICATIONS CATALOG

HEALTH PROBLEMS
MEDICAL CARE
MEDICAL EDUCATION AND HOSPITALS
MEDICAL ECONOMICS

SEND FOR YOUR FREE COPY

BUREAU OF HEALTH EDUCATION
AMERICAN MEDICAL ASSOCIATION
535 NORTH DEARBORN STREET
CHICAGO 10, ILLINOIS

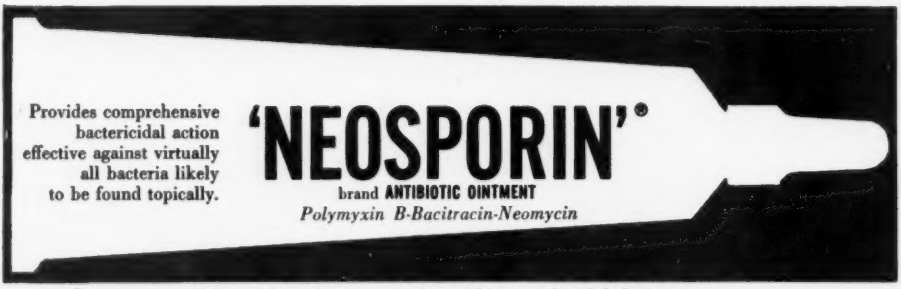

A sense of
well being
for your
PSORIATIC
PATIENT
SOYALOID™
INDIVIDUAL DOME PACKETS
A colloid bath made with the exclusive
Soy Bean Colloid Fraction Component
can produce a truly soothing, emollient effect—
and give the patient a feeling of well being.
A Colloid Bath with all these advantages: no sticki[illegible] fermentation odor—
non-slippery—high in protein value (52% PROTEIN CONTENT)
Supply: Box of 5 packets, 3 oz. each
A most trusted name in Dermatologicals
DOME CHEMICALS INC.
125 WEST END AVENUE, NEW YORK 23
665 N. ROBERTSON BLVD., LOS ANGELES 46
2765 BATES ROAD, MONTREAL
Pat. Pend.

For every topical indication, a Burroughs Wellcome 'SPORIN'...

'CORTISPORIN'®
brand OINTMENT
Polymyxin B-Bacitracin-Neomycin with 1% Hydrocortisone
Combines the anti-inflammatory effect of hydrocortisone with the comprehensive bactericidal action of the antibiotics.

OINTMENT: Tubes of ⅛ oz. and ½ oz. (with applicator tip) for ophthalmic or dermatologic application.

OTIC DROPS: Bottles of 5 cc. with sterile dropper. *Polymyxin B-Neomycin with 1% Hydrocortisone*


Provides comprehensive bactericidal action effective against virtually all bacteria likely to be found topically.
'NEOSPORIN'®
brand ANTIBIOTIC OINTMENT
Polymyxin B-Bacitracin-Neomycin

OINTMENT: Tubes of ½ and 1 oz. and tubes of ⅛ oz. with ophthalmic tip.

OPHTHALMIC SOLUTION: Bottles of 10 cc. with sterile dropper. *Polymyxin B-Neomycin-Gramicidin*

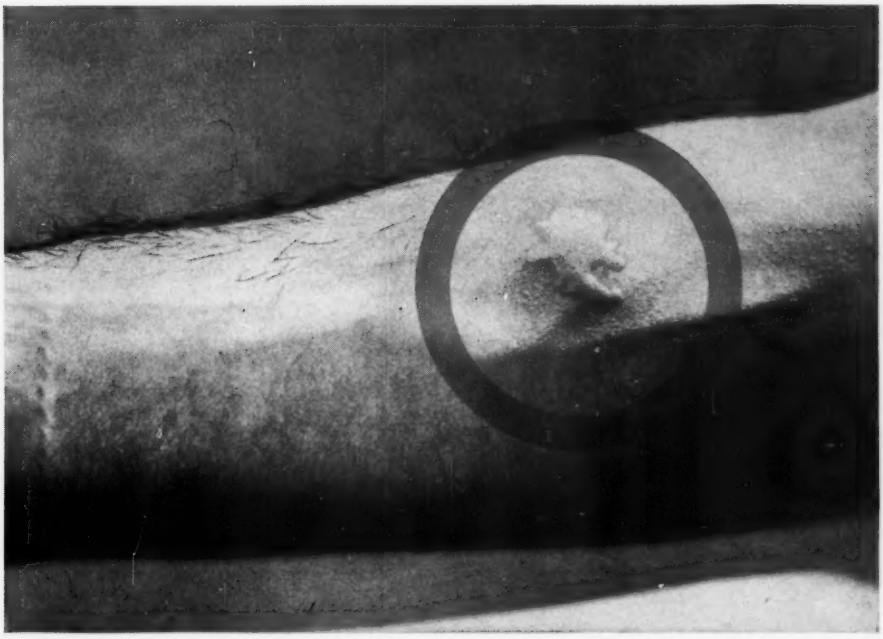
NEW { **LOTION:** Plastic squeeze bottles of 20 cc. *Polymyxin B-Neomycin*
POWDER: Shaker-top bottles of 10 Gm. *Polymyxin B-Neomycin-Bacitracin*

'POLYSPORIN'®
brand ANTIBIOTIC OINTMENT
Polymyxin B-Bacitracin
Offers combined antibiotic action for treating conditions due to susceptible organisms amenable to local medication.

OINTMENT: Tubes of ½ oz., 1 oz. and ⅛ oz. (ophthalmic tip).

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, N. Y.

all-day (and all-night) relief from histamine-caused skin reactions . . .



The vast majority of your patients who suffer from histamine-caused skin reactions get all-day and all-night relief with just one 'Teldrin' *Spansule* capsule q12h. Relief is rapid as well as prolonged, since one third of the 'Teldrin' medication is released within minutes, the rest over a period of 8 to 10 hours. And side effects are minimal.

Available: 8 mg. (for younger children) and 12 mg. 'Teldrin' *Spansule* capsules.

TELDRIN® **SPANSULE®**

brand of chlorprophenpyridamine maleate

brand of sustained release capsules

SMITH KLINE & FRENCH LABORATORIES

Skin deep or deeper?

Certain skin disorders are due primarily to "nerves", others are often aggravated by anxiety, tension, and fear.[1]

'Miltown' therapy, 400 mg. t.i.d., relaxes the mind and allays somatic symptoms of anxiety and tension. It was used with encouraging results in a series of 164 patients with inflammatory skin conditions, including atopic, eczematoid and neurodermatitis, lichen planus, psoriasis, and anogenital pruritus.[2]

'Miltown' has been found "an effective addition to conventional dermatological therapy."[3] Results were achieved "without impairment of physical activity or mental alertness."[3]

References: 1. *Cahn, M. M.: The use of tranquilizing drugs in dermatology. J. Albert Einstein M. Center* **4**:*161, Sept. 1956.*
2. *LeVan, P. and Wright, E. T.: Use of tranquilizers in diseases of the skin—A preliminary report. California Med.* **85**:*87, Aug. 1956.*
3. *Sokoloff, O. J.: Meprobamate (Miltown) as adjunct in treatment of anogenital pruritus. A.M.A. Arch. Dermat. & Syph.* **74**:*393, Oct. 1956.*

Miltown®

meprobamate (Wallace)

WALLACE LABORATORIES, *New Brunswick, N. J.*

TO TREAT

ITCHY, SCALY SCALP

WHICH TENDS TO DRYNESS

sebulex®

ANTISEBORRHEIC SHAMPOO

WESTWOOD PHARMACEUTICALS, Buffalo 13, New York

sebulex®

a therapeutic shampoo
for the treatment of itchy, scaly scalp
which tends to dryness

Stops itching, removes loose dandruff and crusty, matted layers of scales from the scalp through the effective cleansing, penetrating and antiseborrheic actions of *Sebulytic*®, a combination of anionic surface-active cleansers and wetting agents. The antiseborrheic qualities of Sebulytic are further enhanced with the addition of sulfur and salicylic acid. Hexachlorophene provides antibacterial action.

Prevents excessive drying of the scalp through the action of *Kerohydric*™, a crystal-clear, dewaxed fraction derived from lanolin. Kerohydric also leaves the hair soft and more manageable after shampooing.

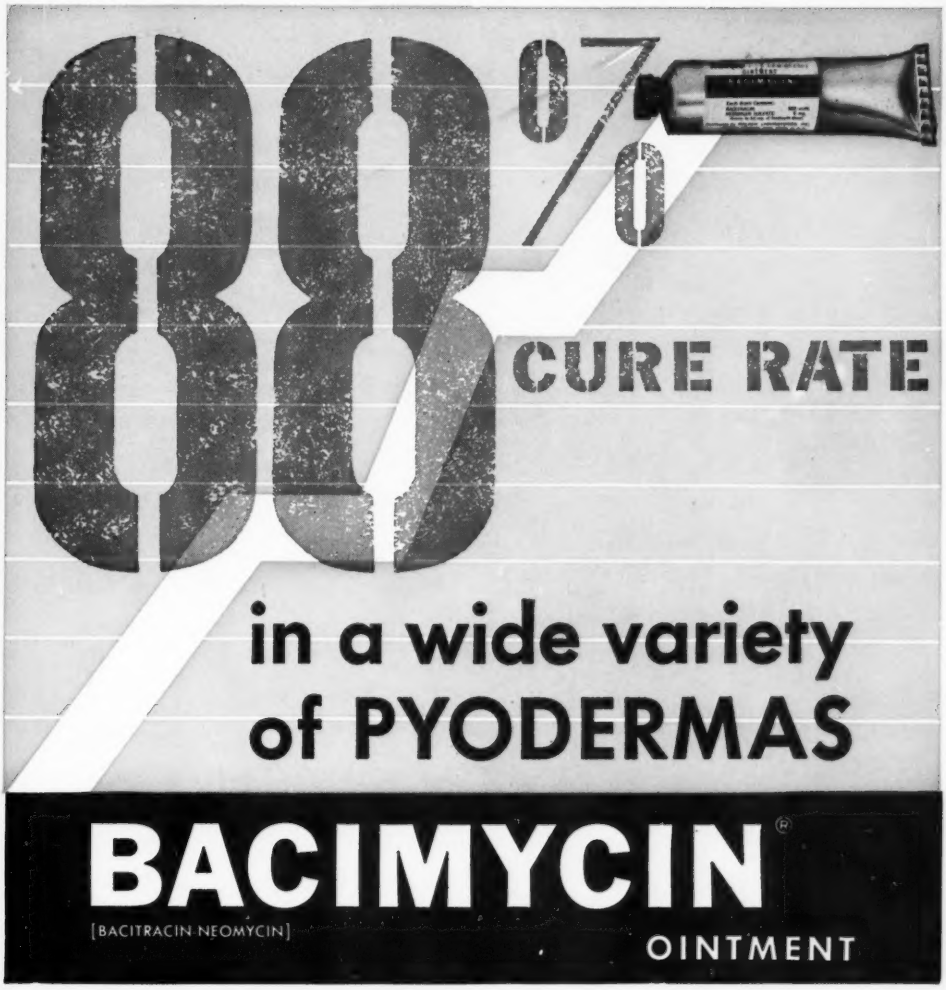
Sebulex is cosmetically elegant. Sebulex meets the up-to-date "cosmetic" requirements for a therapeutic shampoo. It has a smooth, lotion-like texture, an appealing pastel green color, delightful fragrance and produces an abundant lather. Patients like shampooing with Sebulex.

Sebulex does not contain any toxic metallic materials. Thus, it can be used for a prolonged period of time without danger of systemic toxic effects.

Sebulex contains a mixture of anionic surface-active cleansers and wetting agents (Sebulytic). These agents consist of sodium lauryl sulfoacetate, sodium alkyl aryl polyether sulfonate, and sodium dioctyl sulfosuccinate. Sebulex also contains Kerohydric, a crystal-clear, dewaxed fraction of lanolin; sulfur 2%, salicylic acid 2% and hexachlorophene 1%.

Available: In plastic bottles of 4 oz. *Write for samples.*

WESTWOOD PHARMACEUTICALS, Buffalo 13, New York



a first choice for dual antibiotic therapy

In a recent study[1] of 53 patients with various types of pyodermas, the use of BACIMYCIN Ointment "... resulted in a cure rate of 88%...." Impetigo, infectious eczematoid dermatitis, atopic eczema, secondary infections superimposed on dermatitis venenata, and folliculitis were among the common skin infections that showed marked improvement with BACIMYCIN therapy.

BACIMYCIN rarely produces sensitization or primary irritation.

Supplied in ½ oz. tubes for prescriptions; in 100 gm. jars for hospital use; in ⅛ oz. tubes for ophthalmic use. Also supplied as BACIMYCIN with Hydrocortisone, ⅛ oz. tube with applicator tip.

Literature and samples on request.

1. Greenhouse, J. M., and Ryle, W. C.: A.M.A. Arch. Dermat. & Syph. 69:366 (March) 1954.

Walker **LABORATORIES, INC.** MOUNT VERNON, NEW YORK

THE THOUSAND WAYS... AND WHYS... OF

TARBONIS

for unexcelled COAL TAR Therapy

Few medications are more firmly entrenched in dermatologic therapeutics than coal tar. And few indeed have more diverse demands made upon them. TARBONIS, as the sole active agent or as a component of dermatologic prescription formulations, helps to achieve prompt remissions in a wide range of common dermatoses.

TARBONIS, tar therapy unexcelled in performance and acceptability, is a special, refined extract of coal tar in an exclusive vanishing cream base.

UNSURPASSED IN EFFECTIVENESS—promptly relieves itching and promotes healing.

VERSATILE—An excellent vehicle for individualized prescription formulas.

COSMETICALLY ELEGANT—No tarry color, no mess, no stain.

TARBONIS CREAM: 5% Special Coal Tar Extract in an Exclusive Vanishing Cream Base.

Available at all pharmacies on prescription in jars of 2¼ oz. and 1 lb.

REED & CARNRICK · *Jersey City 6, New Jersey*